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## Original Articles

### SURGERY IN AN EMERGENCY

By A. P. MARUFF  
LIEUTENANT, I.M.S.

A SERIES of major surgical operations were performed by the writer with the most gratifying results. Experience revealed that life saving surgical procedures could be performed almost anywhere and with the bare minimum of surgical equipment.

These operations formed the first series of major operations performed in a Persian hospital which had been functioning for six years. No surgical equipment of any sort was available. It was decided to undertake major surgery primarily to save life; the work had its educational value for the local population.

The following operations were performed:—

- |                                     |                                |   |
|-------------------------------------|--------------------------------|---|
| 1. Amputations ..                   | 10 (thigh 4, leg 5, and arm 1) |   |
| 2. Abdominal ..                     | (i) Appendicectomy ..          | 3 |
|                                     | (ii) Splenectomy ..            | 2 |
|                                     | (iii) Vesical calculus ..      | 1 |
| 3. Herniotomy ..                    | 2                              |   |
| 4. Maxillo-facial injuries.         | 2                              |   |
| 5. Gunshot wounds                   | 5                              |   |
| 6. Mastoidectomy ..                 | 1                              |   |
| 7. Filariasis of penis and scrotum. | 1                              |   |

Mortality—one case died.

The operation room was a spare room in the hospital, 12 feet by 8 feet. The operation table was to all intents and purposes a kitchen table.

Surgical equipment consisted of:—

- (i) Carpenter's saw—I.
- (ii) Carpenter's chisel—3 inches broad.
- (iii) Spencer Well's artery forceps—8.
- (iv) Bard Parker handle and a packet of blades.
- (v) Abdominal retractor—6 feet long.

Sterilization was carried out in a Schimmelbusch's sterilizer with two kettles (6 inches by 6 inches) over a primus stove. Suture material consisted of tube catgut, chromic and non-chromic. Silkworm ligatures were hardly used; cotton thread was mostly used. Dressings were sterilized in the Schimmelbusch's sterilizer over a primus stove for over one hour. Cotton thread on its reel was boiled for half an hour. Instruments were 'flamed' before operation. No gloves or gowns were used in the entire series; masks were worn regularly. Tourniquets used were rubber tubing as supplied for enema cans.

#### Amputations

All the cases were very severe injuries due to railroad accidents or heavy loads falling on the extremities. Amputation was imperative to save life, the indication being the complete destruction of the blood supply of the part.

The incisions were not of the textbook type. A circular incision was used with minor alterations to avoid 'dog-ears'. The musculature was

cut down in the line of the incision. No flaps were fashioned. The bone was sawn clean with the carpenter's saw after the muscles had been retracted. The periosteum was not dissected off the bone. Nerves were ignored. The main blood vessels were occluded with transfixation sutures. The muscular flaps were brought together by interrupted sutures. A continuous cotton thread suture was used for the skin. Drainage was never employed.

About 20 grammes of sulphonamide powder were used for each amputation and the powder was liberally applied to the bone ends and muscles before suture. Another layer of powder was applied between the muscles and the skin (see figure 1).

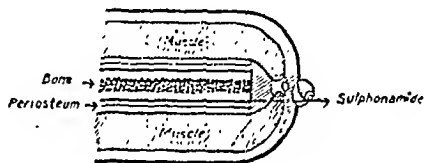


Fig. 1.—Fashioned amputation stump.

Post-operative treatment consisted of draughts of tea well 'sugared' with dates or sugar. No morphia was used in the entire series.

**Results.**—There was no mortality and no sepsis. Post-operative pain was negligible, and wounds healed by first intention.

In five cases in which amputation was performed below the knee, the 5-inch site was selected. This resulted in a well-nourished stump very useful for the type of prosthesis made by the writer. Locomotion was perfect after a month. It is to be noted that exercises were commenced under personal supervision on the third day after operation. The end results were most gratifying because four of the five cases were seen earning an honest livelihood six weeks after operation. The thigh cases had to resort to forearm bearing crutches (see figure 2).

Three amputations in the series were performed without the use of catgut. Cotton thread was used throughout the operation. No sepsis or painful nodules resulted.

The average time for removing a limb was under five minutes, the entire operation was completed in under twenty minutes.

#### Abdominal cases

**Appendicectomy.**—Two cases of acute appendicitis were operated upon. The incision used was the gridiron. Both cases revealed acute suppurative retrocaecal appendicitis. No suppurative peritonitis was associated. Appendicectomy was performed in the classical manner.

Sulphonamide powder about 10 grammes was smeared over the caecum and the appendicular site. The abdomen was closed without drainage. Sulphonamide powder about 5 grammes was dusted between each muscular layer and the skin.



**Results.**—There was no mortality and no sepsis. Patients left hospital on the eighth day.

**Splenectomy.**—The two cases of ruptured spleen were due to direct injury. Diagnosis offered no difficulty. The first case was operated upon four hours after the accident. The patient was in a critical condition. The pulse rate was about 140 per minute. Operation revealed a large malarial spleen, the lower third of which had been completely torn off. The tail of the pancreas was severed. There were about three pints of blood in the abdomen.

Splenectomy was successfully performed. The pancreas was sutured. Fifteen grammes of sulphonamide powder were left in the abdomen over the operation area. The abdomen was closed without drainage. The malarial spleen weighed three pounds.

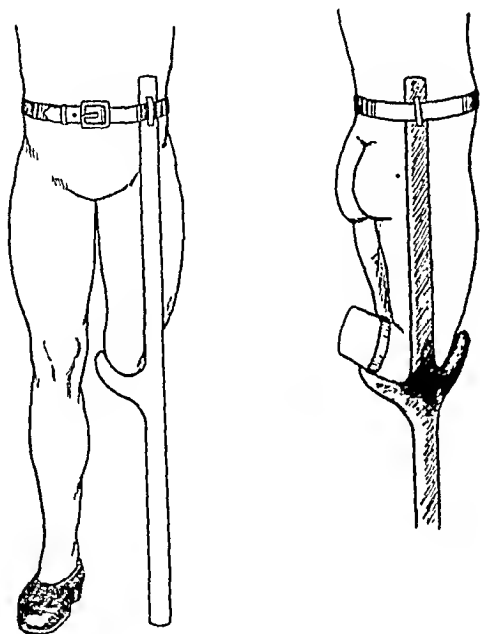


Fig. 2.—Artificial limb.

The peg-leg is placed laterally in line with weight bearing—balance and locomotion are easier than with a central peg-leg. Gait approximates the normal and a walking stick is unnecessary. The belt fixes the upper end of the thigh strut.

The patient died four hours after operation. I am convinced a blood transfusion would have saved his life.

The second case was operated upon 1½ hours after the accident. The pulse rate was 130 per minute. The operation revealed a severely lacerated spleen. Intra-abdominal hæmorrhage was marked. The spleen was large; hence, a linear incision could not be used. The pancreas was severed at the junction of the body and tail. Splenectomy was performed and the pancreas sutured with chromic catgut; the tail of the pancreas was excised. Fifteen grammes of sulphonamide powder were left in the abdomen over the operation area. The (malarial) spleen weighed 8 pounds.

This patient made an uneventful recovery. One wonders how long he will live without his spleen in a highly malarious locality.

**Vesical calculus.**—The patient was seen with typical signs and symptoms of intestinal obstruction. Rectal examination revealed a hard mass situated anteriorly. Pressure on the mass resulted in severe pain at the tip of the penis. The urinalysis revealed pus.

The bladder was opened and a large calculus removed (see figure 3). The bladder contained frank pus. The bladder was closed with catgut and the wound with cotton thread without drainage. Ten grammes of sulphonamide powder were placed in the operation area between the bladder and the skin. A catheter

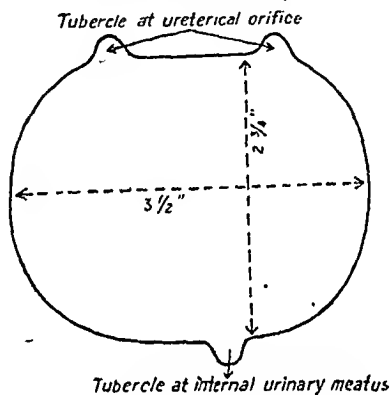


Fig. 3.—Vesical calculus.

The stone was impacted over the Trigone. Bilateral hydronephrosis must have been associated.

was retained in the urethra for two days. The patient made an uneventful recovery and left hospital on the eighth day.

#### Herniotomy

The patient had a complete indirect inguinal hernia on both sides. He desired operation because he could not earn his living as a labourer.

The right sac revealed the appendix adherent to it. Appendicectomy was performed. The sacs were completely dissected and excised. No canal repair was undertaken. The muscles were in excellent condition. The wounds were closed without drainage. The patient was kept three weeks in bed. The wounds healed by first intention. He was seen five months later at work; there was no evidence of a recurrence.

#### Maxillo-facial injury

The first case was a gunshot wound on the face. The bullet entered below the infra-orbital foramen; the exit wound was ½ inch below the tragus. The lobe of the ear was shot off. The bullet track was excised, the antrum exposed and all loose bone fragments removed. The lower third of the parotid gland was involved. It was excised in the line of the bullet track. There was no alarming hæmorrhage. The

antrum was filled with 10 grammes of sulphonamide powder. The wound was packed with sulphonamide powder and closed without drainage. The patient made an uneventful recovery. The wound healed by first intention. No parotid fistula developed. When seen a month after the operation the patient had no complaints. The maxilla was healthy, the scar being barely perceptible.

The second case was the result of a direct injury. A wooden pile weighing about a ton struck the patient's face on the left side. There was a compound fracture of the facial surface of the maxilla. The nose was completely disfigured.

The wound was excised, and all loose bone fragments were removed. The antrum was packed with 10 grammes of sulphonamide powder. The wound was dusted with sulphonamide powder and sutured.

The nose was refashioned by manipulation and intranasal leverage.

The wound healed by first intention. The patient when seen six weeks later had no complaints; the nose was a good-looking one.

*Gunshot wounds.*—Five gunshot wounds of the extremities were operated upon. All were wounds without bone, nerve, or major vascular lesions. The bullet track was excised—excision in its true meaning. The wound was packed with 15 grammes of sulphonamide powder and closed with a continuous suture without drainage. All wounds healed by first intention.

*Mastoidectomy.*—The patient had acute suppurative otitis media on the right side. Mastoiditis was associated. Oedema was demonstrated from occiput to forehead up to the vertex.

The mastoid process was excised as far as possible clear of pus. The antrum and aditus were cleared. The middle ear was full of pus with the ossicles 'floating' in pus. The bone was smoothed out till clear healthy bone was reached. The lateral sinus was exposed for about an inch. It was healthy. The wound was packed with 15 grammes of sulphonamide powder.

The wound was drained. The drain was removed on the second day. The wound healed by first intention. The patient left hospital on the eighth day, completely cured. There was no facial paralysis, giddiness or discharge from the ear.

A carpenter's 3-inch broad chisel was the chief instrument used. A small everyday hammer was used.

A case of *filariasis of the penis and scrotum* was brought up for surgical aid. The patient showed suicidal tendencies.

The penile skin and the scrotum were excised; the tunica vaginalis of right and left sides was excised. The testicles were embeded under the fascia lata at the upper end of the thigh medially. The skin off the thigh was Thiersch grafted on the penis with the Bard Parker knife. The result was most gratifying. The graft took, and there

(Concluded at foot of next column)

## INGUINAL HERNIA

(A RECORD OF 104 CASES)

By N. DAS, M.B.

Assistant Surgeon, Emergency Hospital, Feni

BASSINI published his operation for inguinal hernia in 1884. It soon became the standard operation. Operations at present in use are all based in principle on Bassini's operation.

(Continued from previous column)

were no complications. The patient was a new man with a happy future. A grateful patient has been left behind in Persia. This patient has never left Persia. He has had filariasis of the scrotum for eight years. He has been in service as a cook with a Bengali for two years and a Madrassi for three years during the last eleven years.

*Culex fatigans* is found in South Persia. This possibly explains the occurrence of filariasis. Will filariasis spread with the Indian Army?

*Discussion.*—The operations detailed cover a varied field. It is to be noted that sepsis is conspicuous by its absence considering the conditions, locality and the personal hygiene of the patients. Undoubtedly sulphonamide locally has played the star rôle. One could without hesitation recommend its use as detailed where sterility is doubted.

The equipment is interestingly limited. The carpenter's saw was an excellent instrument. Manipulation is easy and the speed with which a femur can be sawn through is amazing.

The carpenter's chisel was 3 inches broad, and sharp. My chief, Major Drummond, I.M.S., always recommended its use in orthopaedic surgery. The instrument proved its value in an emergency.

The limited use of catgut definitely minimizes sepsis. It is used where essential. In the scrotal tumour case, only one tube of the catgut was used.

Drainage was not used except in the mastoidectomy. The dictum 'when in doubt don't drain' is borne out in this short series.

The instruments were used only for 'clean cases'. They were boiled once a week and looked after with affectionate care. They were sterilized before the operations by 'flaming'.

No morphia was used in the series. Patients could not afford it; it was not essential. A plaster was always used to protect the wounds till the sutures were to be removed. Chloroform and ether were used, 'the bottle and rag method'; it proved its value in the emergency. Dates provided an abundant supply of glucose and vitamins A and D.

Gratitude must be expressed to my very able assistant, Sgt. C. R. Pritchard, R.A.M.C., for his never failing co-operation and untiring enthusiasm. He had never seen an operation till he joined the unit. He has developed into an excellent assistant. The writer thanks Capt. T. W. Percival, R.A.M.C., for the anaesthesia given well.

Almost every year new modifications are described. Why? It is because hernia not infrequently recurs after operation. Why does hernia recur? Suppuration was alleged as the cause, but it has been proved that suppuration occurs in less than one-fifth of the recurrent cases (Battle). Incomplete removal of the sac is an important cause of recurrence. The neck should be properly identified and the sac transfixed just proximal to it. Unless this is done thoroughly, a dimple at least will be left at the neck of the sac and it will form the precursor of the future sac. Loss of tone of the muscles or their actual degeneration constitutes another important cause of recurrence. The muscles at fault are the internal oblique, the transversalis and the aponeurosis of the external oblique. Other causes of recurrence which need a reference are trauma, faulty technique, lack of co-operation of the patient, and persistent and violent expulsive efforts caused by conditions such as chronic cough, enlarged prostate, obstinate constipation, etc. It goes without saying that these latter troubles need rectification before the cases are actually put up for operation. The loose areolar tissue under the aponeurosis of the external oblique at the site of operation and around the cord should be broken or removed by gauze dissection, because this areolar tissue helps recurrence by keeping an open space under the external oblique. Sixty-five per cent of recurrent hernias occur within 6 months, and 85 per cent within 12 months after operation (Coley).

This paper gives a record of 104 cases, all seen in the district of Bakarganj (Bengal) and operated on in the Barisal Sadar Hospital. Cases were operated on at all ages and at all stages; in other words, all cases in which there was a reasonable prospect of success were done. The only cases which were left out as inoperable were obese and elderly patients in the advanced stage of secondary weakness of musculature. The results have so far been satisfactory.

Of these cases, 68 were indirect, 25 direct and 11 congenital. Fifty-five cases of indirect hernia occurred in persons between 20 and 45 years of age. Eight cases of direct hernia occurred between 30 and 45 years and 12 between 50 and 62 years of age.

TABLE I

Age in years	Number of cases	Indirect	Direct	Con-genital	Duration of disease in years
5	1	..	..	1	4
12-16	10	2	..	8	3-4
20-30	44	38	4	2	5-8
30-45	27	19	8	..	5-8
50-62	20	8	12	..	12-15
80-88	2	1	1	..	10-20
TOTAL	104	68	25	11	

About 75 per cent of the patients were Hindus and 25 per cent Muslims. It might be mentioned that Bakarganj is a Muslim majority district. The comparative muscular weakness of the Hindus was the only noticeable cause for the preponderance of hernia in this community.

TABLE II

Age in years	Number of cases	Hindu	Muslim	Christian
5	1	1	..	..
12-16	10	8	2	..
20-30	44	32	12	..
30-45	27	20	7	..
50-62	20	15	5	..
80-88	2	1	..	1
TOTAL	104	77	26	1

### Operation

In this small paper it has not been my aim to describe the operative details extensively, nor do I think it would serve any useful purpose. Stress has been laid on those points which were found to be particularly important in preventing recurrence. I have described the operation under three heads—indirect, direct and strangulated hernia—and have incorporated notes of a small number of cases which I thought were worthy of separate mention.

*Anæsthesia.*—Fifty-six cases were done with spinal neocaine (0.5 to 1.0 gramme). It was found to be a very useful and safe anæsthetic. Unfortunately, it is not available now. Thirty-three cases had A.C.E. In 15 cases in old persons, subjects of chronic bronchitis or 'bad risk' cases, operation was done under local novocaine 1 per cent.

*Technique of local anæsthesia.*—One 10 c.cm. syringe and a 3½-inch needle are necessary.

(a) Through a point 1 inch medial to the anterior superior iliac spine, the muscular planes are infiltrated, the ilio-inguinal, the ilio-hypogastric and the twelfth dorsal nerves being thus blocked.

(b) Through a point at the saphenous opening, tissues below the inguinal ligament and at the base of the scrotum are infiltrated, the pubic and the genito-femoral nerves being thus blocked.

(c) Through a point in the external ring, the middle line, the neck of the scrotum and the neighbourhood of the inguinal canal are infiltrated.

(d) The line of skin incision is infiltrated.

*Indirect inguinal hernia.*—An incision is made over the inguinal canal extending from an inch outside the abdominal inguinal ring to just short of the pubic spine. The skin, the fascia of Camper and the fascia of Scarpa are successively cut, and the aponeurosis of the external oblique is exposed and split in the line of its fibres from the external ring outwards. The two

flaps of the external oblique are reflected to expose the conjoint tendon and the deep surface of the Poupart's ligament clearly. The ilio-hypogastric nerve which runs over the conjoint tendon is carefully preserved. The ilio-inguinal nerve which runs with the cord is also safeguarded.

By a few light touches of the scalpel over and along the cord, the sac can be found as a shining membrane; it is caught with a pair of artery forceps and is separated from the cord to just beyond its neck. Recognition of the neck is very important because incomplete removal of the sac is a very important cause of recurrence. The neck should be properly identified and transfixed just proximal to it. How can one identify the neck? At the neck (a) the sac expands into the peritoneum, (b) there is a collar of fat (extra-peritoneal), (c) the sac is narrowest and thickest and (d) the inferior epigastric artery courses round the sac. But the sac should not be pulled beyond the neck as in that case one is likely to encounter the bladder. The sac is then opened to make sure that no adhesions between the sac and its contents exist. The neck is transfixed with catgut no. 2 and the sac is cut away. In nearly 50 per cent of cases of the present series, the cremaster muscle was seen rather overgrown and was removed between ligatures with a view to giving less bulk to the cord and less width to the ring to be constructed to give passage to it.

The conjoint tendon is then sutured to the deep aspect of Poupart's ligament by 4 or 5 interrupted stitches of chromicized catgut no. 3. One of the stitches is placed above the abdominal inguinal ring (Coley's stitch) and others below it. The uppermost of the stitches below the cord is applied so as to leave just enough room for the cord, i.e. the cord should neither be compressed nor left loose. The lower stitches are applied behind the cord. Great care is taken in picking up Poupart's ligament, so that this delicate structure is not lacerated. These stitches, if tied too tight, are likely to strangle and damage the muscular fibres of the conjoint tendon and lead to stitch abscess, one of the causes of failure. In order to produce as little damage as possible these sutures are placed at right angles to these structures.

In the vast majority of cases, recurrence occurs through the lower end of the canal, and this part of the canal, therefore, needs special attention. The reflected inguinal ligament is a fan-shaped expansion from the lacunar ligament and proceeds medialwards behind the spermatic cord and superior crus of the subcutaneous inguinal ring and in front of the inguinal aponeurotic falx to its fellow of the other side. The reflected inguinal ligament and the inguinal aponeurotic falx are sewn behind the cord to Poupart's ligament close to its insertion into the pubic spine.

*Repair by hernial sac.*—Heterogenous tissues, viz, the muscular fibres of the internal oblique and the transversalis and the ligamentous Poupart's ligament, do not unite or the union is insecure, a fact familiar to all who have had occasion to operate on recurrent hernias. Moreover, these structures can only be apposed by stitches under some tension, and tension stitches do not take. These factors baffle Bassini's primary object of strengthening the posterior wall of the inguinal canal. Moreover, the normal sphincter action of the conjoint tendon and the arched fibres of the internal oblique which function by contracting down on the cord and Poupart's ligament is interfered with. Living fascia is thus introduced to repair the canal (Gallie).

Fascial strips are cut from the fascia lata and are laced or darned as a suture across the gap of the posterior wall of the canal. A strip of aponeurosis detached from the upper of the external oblique flaps at the site of the operation is also used as living suture. It is freed at its lateral end and left attached at its medial end and used as a continuous suture approximating the conjoint tendon and Poupart's ligament.

In the present series in almost all the cases the duration of illness was 5 years or more and the sacs were fairly thick. Strips were cut from the sac and made use of as living suture in the repair of the

inguinal canal. The sac after excision is kept in sterile normal saline at body temperature. It is laid open longitudinally and made into a long strip half inch wide by cutting the sac in a circular fashion from near the margin towards its centre. It is then threaded on a large-eyed needle (of Gallie) and used as a continuous suture, picking up in turn the lower edge of the conjoint tendon and the deep aspect of the Poupart's ligament, to lace across the posterior wall of the canal. It is next carried round the cord to constrict the abdominal inguinal ring. The end of the strip is stitched to the penultimate loop of the suture by catgut. Great care is taken in picking up Poupart's ligament so that the delicate structure is not damaged. It is essential to apply the living sutures after the tension is relieved by interrupted catgut stitches. A few catgut stitches are applied fixing the angles of the continuous suture to the conjoint tendon. The vas and the cord are then placed on the sewn conjoint tendon and the flaps of the external oblique aponeurosis are sutured over it by interrupted chromicized catgut no. 1. The skin is then sutured without drainage by interrupted silk or silkworm gut.

### *Direct inguinal hernia*

The operation for direct hernia differs from that for oblique hernia in that the repair of the canal must be more thorough because the musculature is defective.

The internal oblique and transversalis are degenerative, the conjoint tendon atrophied and stretched and the external oblique aponeurosis toneless and frayed. The sac is almost always a peritoneal bulge and on account of the relaxed condition of the surrounding structures the bladder is frequently associated with the sac. In the present series in almost all of the 25 cases, the sac had a wide neck and could not be tied in the ordinary way. It was opened, the edges excised and then united by a running suture of chromicized catgut no. 2, like a laparotomy wound. The strip of the sac like that described in oblique hernia is laced across the posterior wall of the canal. It is then carried beyond the cord through the external oblique aponeurosis to secure closure of its gap in front of the cord.

*Post-operative care.*—Nothing special. Stitches are removed on the eighth day. Period of stay in bed should be 3 weeks. Sedentary workers may resume work after a further 3 weeks' convalescence but must be warned to avoid any work of strain for several months. Labourers should avoid heavy work for 6 months. All the cases of this series had an uneventful convalescence.

Of the 25 cases 6 were recurrent hernia. Hernia recurred in 3 cases within 7 months of operation and one of these 3 cases was a recurrent hernia.

### *Strangulated inguinal hernia*

The operative procedure is similar to that of internal herniorrhaphy with modifications that may be necessary according to the condition of the strangulated loop.

The sac is exposed, its tense fundus nicked to let out the pent-up collection of fluid which is mopped up carefully and the opening is enlarged up to the neck. Contrary to the teaching of the textbooks, it is always seen that the constricting ring is the fibrous thickened neck of the sac at the internal ring which by itself has nothing to do with strangulation. The constricting ring is divided with great care to avoid injury to the strangulated gut which is then drawn out to determine its viability.

There were 33 cases of strangulated hernia in this series and 32 were of indirect variety and one of direct. From the standpoint of treatment the cases could be divided into 3 groups

according to the condition of the strangulated intestine, viz, viable, doubtful and non-viable.

TABLE III

*Difference between viable and non-viable gut*

	Viable	Non-viable
1. Colour	Pink and sheeny.	Grey and lustreless.
2. Feel	Elastic	Toneless and flaccid like sodden blotting paper.
3. Peristalsis	Present	Absent.
4. Wrapped in hot packs for 5 mins.	Return of colour and tone.	Unchanged.
5. Pulsation of mesenteric vessels.	Present	Absent in late cases.
6. Fluid of the sac.	Clear and odourless.	May be sanious and offensive.
7. Inhalation of pure oxygen.	Colour rapidly turns healthy pink.	Color unchanged.

A. *Viable*.—Twenty-six cases. In each the gut was viable beyond all suspicion and the hernia was dealt after relief of strangulation in the ordinary way.

Two cases are worthy of mention.

A Brahmin, aged 88 years. Right inguinal hernia—20 years. Operated on 6 hours after strangulation under local novocaine 1 per cent. The canal was repaired with sac as usual. Fourteen months after operation he died of malignant ulcer of the tonsil but there were till then no signs of recurrence of hernia.

An English priest, aged 80 years. Had strangulation of a recurrent inguinal hernia and was operated on 4 hours after strangulation under local novocaine 1 per cent. It was a direct hernia. Ten months have elapsed after operation but there is as yet no sign of recurrence.

B. *Doubtful*.—Only one case.

Hindu male, aged 30 years. Operated on 9 hours after strangulation. The gut was retained outside the abdomen, after release of the strangulation, by fixing the gut to the neck of the sac by a few catgut sutures. The gut was kept covered with gauze soaked in hot water, frequently changed. The gut showed definite signs of recovery after 24 hours when the sutures were removed and the prolapsed intestine was reduced. The sac was transixed and cut away as usual. It was washed in saline, cut into a long strip and utilized to effect a radical cure in the repair of the canal. Stitches were removed after 7 days. Primary union.

C. *Non-viable*.—There were 6 such cases. One case had gangrene of the proximal loop at the ring of constriction, which was buried by interrupted catgut sutures and the loop returned into the abdomen. The canal was repaired with sac as usual.

In 3 cases there were patches of gangrene chiefly in the anti-mesenteric border of the herniated gut. These patches were infolded by purse-string sutures and the gut returned into the abdomen. The canal was repaired with sac as usual.

Two cases showed definite gangrene of the ileum and one came 4 days and the other 10 days after strangulation.

The former, a Hindu male, aged 28 years, was in fairly good general condition. The gangrenous gut was

resected and an end-to-end anastomosis done. It was then returned into the abdomen and the canal repaired with the sac as usual. He had an uneventful recovery. The other patient, Hindu male, aged 36 years, was highly toxic and exhausted by pain, vomiting and sleeplessness. The operation was conducted under local novocaine 1 per cent. The ring of constriction was divided and the loop drawn down and sutured to the sac near its neck by interrupted catgut stitches. The two limbs of the loop were then sewn together by a few stitches above the gangrenous portion (6 inches) which was next cut away. A large rubber tube was passed into each limb of the loop and sutured in. An artificial anus was thus made. The operation was done very quickly and his general condition received all attention. Gradually he improved and on the 7th day was given rice diet. On the 14th day a secondary operation was done to close the faecal fistula. Ten days later he was operated on for the third time. The sac was slowly and carefully dissected out, transixed at the neck and cut away. The canal was repaired as in Bassini's operation, no attempt being made to utilize the sac in suturing. The reinforcement of the posterior wall was done by a quadrilateral flap cut from the anterior wall of the rectus sheath with its base at the outer border. This flap was turned down and sewn to the Poupart's ligament, the attached edge acting as hinge (Walfer). At each step of the operation sulphonamide powder was liberally dusted and the skin sutured without drainage. The patient, who could not be more ill than he was, survived this gravest emergency only because the absolute minimum was done at the first operation and the whole procedure was split up into 3 stages.

TABLE IV

Type	Number	in Recurrence 7 months.	CURE FOR			
			4 years	3 years	2 years	1 year
Congenital ..	11	..	4	3	2	2
Indirect ..	35	..	7	12	10	5
Direct ..	19	2	5	4	7	2
Recurrent (direct) ..	6	1	1	3	1	..
Strangulated ..	33	..	9	13	8	3
TOTAL ..	104	3	26	35	28	12

*Discussion*

Half a century ago Bassini observed: 'It will appear excess of daring to write at the present day of the radical treatment of hernia.' It must be admitted that even today, certain cases recur after operation.

In the present series, every one who had any prospect of cure was given a chance and the results were unexpectedly good. Except one case of congenital hernia in a child and another case of a very bad strangulated hernia, the inguinal canal of every other case was repaired by living suture derived from the sac which, being old-standing, was thick-walled.

In not a single case of the whole series did the sac-suture fail to take, probably because it was placed more or less in the original and natural position of the sac from which the suture was derived. When strips of fascia lata are

(Concluded on opposite page)



## RESECTION OF THE RIGHT HALF OF THE COLON (HEMICOLECTOMY)\*†

By S. D. ARAWATTIGI

Surgeon, Miraj Medical Centre, Miraj (S.M.C.)

### Introduction

SURGERY of the colon proper necessarily awaited full development until the Listerian era,

(Continued from previous page)

used, an additional operation is necessary and extra time is lost in suturing the wound on the thigh. In repair by aponeurotic suture, there is a chance of weakening this essential structure, and the strip that is derived from it is obviously not long enough. Moreover, when the musculature is defective, the external oblique aponeurosis is too thin to provide a suture. The sac, to be useful as suture material, must be thick, and I have used it with extremely satisfactory results in old-standing cases of inguinal hernia.

Three cases recurred, 2 direct and 1 recurrent. Advanced muscular degeneration and loss of tone were the evident causes of recurrence which appeared within 7 months of operation. A case of bilateral recurrent hernia has apparently been cured, there being no signs of recurrence for 2 years on one side and 1 year on the other. Even strangulated hernia cases did very well with this procedure. The idea of utilizing the sac of the hernia as living suture owes its origin to my professor, Dr. S. Dutta, F.R.C.S. (Edin.), whom I assisted in 1933-35 in operations of inguinal hernia done in this way. I do not know nor have I read of any other surgeon making use of the sac in the repair of the inguinal canal in operations for hernia. Though the number of cases in the present series is too small to assess the efficacy of this method, yet I feel that suturing the posterior gap of the canal with the sac has a definite place in the treatment of inguinal hernia. It goes without saying that the sac should be transfixed at the proper site, without which failure is very likely to occur.

### Summary

1. One hundred and four cases have been recorded.
2. Causes of recurrence of inguinal hernia have been discussed.
3. The sac has been utilized as living suture in repairing the canal, with promising results.
4. Thirty-three cases of strangulated hernia are included and their treatment discussed.

I am indebted to Rai B. B. Hajra Bahadur, Civil Surgeon, Bakarganj, for permitting me to operate on these cases and publish this paper.

\*Read before the 9th General Conference of the Christian Medical Association of India, Burma, and Ceylon, on 26th March, 1943, held at Vellore (South India).

†This article was accompanied by a very large table giving a full detail of all the 40 cases. This table we are unable to reproduce.—EDITOR, J. M. G.

which followed the discovery of anaesthesia, and permitted fearless invasion of the peritoneal cavity. In the beginning, colostomy as a decompressive measure was the only operation performed for cancer, but gradually enterprising and persistent surgeons doggedly extended the horizon and began to attempt the removal of malignant lesions and the establishment of the gastro-intestinal continuity.

As far back as 1823, Reybard successfully resected the sigmoid flexure for cancer, and made a primary anastomosis in a young man of 23 years. The patient recovered, but professional criticism served to discourage the popularity of so drastic a measure. The progress was slow thereafter. Again in 1843, Thiersh resected the colon for acute obstruction. Thirty-seven years later, only 10 resections of large bowel had been recorded and only 3 of these were successful. Later, however, more resections were performed with great success because of the development of the 'principle of exteriorization' (Mikulicz's). Due to the efforts of many bold and enterprising surgeons such as Billroth, Marshall, Kraussold, Block, Mikulicz, Weir and many others, colonic surgery opened up a new field for extensive and successful resections.

The exteriorization principle was first advocated by J. M. Borton of Philadelphia in 1888 in '13th resection at the ileo-caecal valve for epithelioma'. Subsequently Block in 1891 published a report of this type of resection; and many others described similar procedures during the following years.

In 1902 Mikulicz spoke of a procedure which he claimed to have performed first in 1886 and for some reason his name has been commonly attached to all exteriorization operations by the surgeons of America. To-day the scope of application of operative procedures to many lesions of the large bowel hitherto considered ill-fitted for surgery has been enormously broadened. It is true that any mutilating operation is a most unpleasant duty to perform, yet in dealing with the diseased part of the bowel where irreparable damage has taken place, such as in cancer threatening life, destructive and mutilating methods which may prove to save lives in a large percentage of patients must be accepted and adopted.

Although, theoretically, total extirpation of the colon is probably the operation of choice, this procedure is associated with too high a mortality to be of practical value. Subtotal colonic resection of the greatest possible portion of the colon, including a part of the ileum and the involved lymph nodes with mesentery, gives the best results. It is true that in advanced cases in which the malignancy has invaded the other surrounding structures, with metastases in the liver and other parts of the abdomen, the above resection is obviously a palliative procedure. It removes the ulcerating, bleeding, obstructive or painful tumour, and lengthens life, but does not

give a permanent cure. After the operative measure the residual tissue may be subjected to radiation. When the growth is strictly confined to a part of the colon, a sub-total resection with the involved mesentery is a curative procedure, though a post-operative radiation may also be required.

#### *Present work*

The object of the present investigation is to modify the technique of sub-total resection of the colon, and to apply this measure of treatment in all pathological conditions involving the colon. It has also been the aim of the author to simplify the procedure, so that the mortality rate may be reduced. The advisability of doing the resection in one or two stages is also fully discussed.

One must carefully consider whether resections of the large intestine should be done in one or two stages. Most surgeons consider a two-stage operation as a safer procedure from the standpoint of operative mortality; and statistics from various hospitals and clinics seem to bear this out. Bieren (1941) reported during a period of 17 years (1922 to 1939) 40 cases of adenocarcinoma of right colon, out of which only 11 were operable; 7 were done in one stage with a mortality of 43 per cent and the remaining 4 in two stages with a 25 per cent mortality. Ransom (1939) reported a mortality rate of 32 per cent for the one-stage operation in contrast to a mortality rate of 20 per cent for the two-stage operation. Allen (1937) reported a mortality rate of 20.5 per cent for the one-stage operation in 73 cases of carcinoma and a mortality rate of 11 per cent for the two-stage operation in 18 cases. Pemberton and Whittaker (1937) reported 46 cases; 8 cases were treated in one stage with 1 death, a mortality of 12.5 per cent, and 38 cases in two stages with 2 deaths, a mortality rate of 5.2 per cent. There were 2 deaths out of 5 cases treated with ileo-colostomy. Harvey (1934) reported 18 cases with a mortality of 11 per cent from a one-stage operation. Stone and McLanahan (1939), Lahey (1939) and others advocate the one-stage operation and record a mortality rate as low as 11 per cent.

Mayo and Lovelace (1941) argue that, irrespective of the few advantages of the one-stage operation, the two-stage operation is in some ways advantageous in minimizing the mortality rate. The most important advantage of the one-stage operation in case of neoplasm, in his opinion, concerns the factor of time. They state: 'it is reasonable to suppose that the longer the malignant lesion remains in the body the greater is the risk of extensive metastases which will preclude resection'.

There are several factors involved in the mortality rate of resection of the large bowel as compared to that of the small bowel. Minor soiling of the peritoneum with the contents of the stomach, duodenum, jejunum, or ileum, while it is to be avoided, does not carry the grave

danger of spreading peritonitis as does a contamination from the large bowel. Similarly relatively gross interruptions of the blood supply in the stomach or the small intestines, where the anastomotic circulation is profuse, do not cause the same danger of necrosis as in the large bowel where the interruption of a single terminal vessel may at times lead to a localized ischæmia at the suture line. Again the wall of the colon is of a thinness which allows a smaller margin of safety in placing of the suture and in its holding power. It is apparent that, although the large bowel seems to be a grosser structure than the small bowel, surgical manipulations of it require a more faultless technique. This may be the reason why exteriorization was practised in the earlier days of colonic surgery.

The basis of this study has been a series of 40 cases in which resection of the right half of the colon was performed by the writer during the past 6 years. In 9 cases a two-stage operation was performed without any death. (The first stage of the last case was performed by the other surgeon of this hospital.) Thirty-one cases were treated by the one-stage method, with 2 surgical deaths—one on the second day and the other on the third day after operation. (There was another death which cannot be considered as directly due to operation, as the patient died 6 months later after a long illness with many complications.)

#### *Operation*

*Indications.*—Indications for the resection of the right half of the colon were formerly confined to the malignancies. Now, with the perfection of the technique, this operation may be employed for conditions such as growths benign and malignant, tuberculosis, non-specific granuloma involving the ileum and cæcum, chronic ulcerative colitis and actinomycosis. My series of 40 cases consists of 1 of carcinoma of cæcum, 3 of carcinoma of the hepatic flexure, 1 of carcinoma of the ascending colon, 1 of lymphosarcoma of the ileum and glands, 10 of tuberculosis of the cæcum and ileum, and 24 of regional enterocolitis.

*Pre-operative care.*—I consider that a post-operative building up of the patient's strength is more important than a pre-operative care, because tonics, etc., do not help the patient, as he is unable to assimilate due to obstructive lesions. Pre-operative preparation need not be resorted to as a routine, but it may be confined to patients whose general health is very poor. Blood transfusion, whenever available, should be given before the operations, as it definitely lowers the mortality rate. It may be noticed that a lady aged 24 years, emaciated, anæmic, weighing 54 pounds, with tuberculosis of the cæcum, was operated on successfully in one stage after blood transfusion (case 9). Three more cases in which the general condition was very poor received blood transfusions before operation, with much benefit. The weight of most patients

varied between 70 and 80 pounds and the average hæmoglobin percentage was 50. In spite of the poor general condition of many patients, they stood the one-stage resection well. The patient should not be subjected to unnecessary pre-operative restrictions in diet, or to cathartics. Garlock and Ginzburg (1943) and Glass advocate cleansing of the bowel by mild purgatives, colonic irrigation, the use of the Miller-Abbott's tube, and the routine pre- and post-operative administration of sulphanilamide. These measures were omitted in this series, with no ill-effects. One should be exceedingly cautious in the use of the Miller-Abbott's tube and in the administration of sulphanilamides as a routine.

*Anæsthesia.*—Spinal anæsthesia is the anæsthesia of choice. It gives good relaxation and prevents manipulative shock. Patients stood the anæsthesia well. I used neocaine in 13 cases and stovaine in 22 cases. In some cases I had to use either intravenous morphia or general anæsthesia (C&E) towards the end when the operation was prolonged. For 5 cases, when the general condition of the patient was very poor, local anæsthesia was used and supplemented by either intravenous morphia or general anæsthesia.

### Technique

*Incision.*—The right pararectus incision, which has the advantage of direct access to the right half of the colon, is the most suitable one. When the abdomen is opened, a careful exploration is made to determine the nature, extent and operability of the lesion.

*Mobilization of the ascending colon.*—The peritoneal cavity is packed and a self-retaining retractor is inserted. The loop of the hepatic flexure is pulled up by passing a gauze piece through the mesentery. The two layers of the mesentery are separated by passing the fingers between the layers through the perforated mesentery. Divide only the lateral peritoneal reflection of the right half of the colon just lateral to the lateral border of the ascending colon and cæcum, up to the lower border of the cæcum, bearing in mind the ureter, the duodenum and the pancreatic duct, which lie in close relation to the ascending colon. (The last structure was once accidentally caught in the clamp and divided. Such an injury to the duct must be attended to by transplanting it into the duodenum.) Then free the required segment of the mesentery of the involved terminal ileum. Reflect the whole mobilized segment of the bowel towards the midline over the abdomen. Further separate the gut from its posterior minor attachments, including all the enlarged lymph nodes, and cut the medial layer of the mesentery.

*Hæmostasis.*—Perfect hæmostasis should be accomplished by transfixing and ligating every bleeder separately, starting from the ileal mesentery and continuing towards the transverse colon in both the layers of the mesentery.

*The resection of the mobilized segment.*—A rubber-covered anastomosis clamp is placed over the ileum proximal to the level of resection, and a crushing clamp at the distal level, and the gut is divided by an electric knife. Similarly the transverse colon is divided at the junction of its medial one-third and lateral two-third.

*Anastomosis.*—An end-to-end anastomosis in every case was made because this type of anastomosis maintains the natural continuity of the intestinal tract. Slight constriction of the lumen may sometimes function as a valve. Usually the terminal ileum is dilated and so there is no disproportion in the size of the colon and ileum. If the ileum is found to be narrower than the colon, a small slit at the anti-mesenteric border, or an oblique cut, will rectify such a technical difficulty. As regards suture material, catgut was used throughout. My experience with cotton in other cases was not very encouraging. I used silk in two cases when the proper size of catgut was not available.

*Peritonization.*—The deperitonized area is closed by bringing the two edges together. Likewise the mesenteric edges of the ileum and transverse colon were sutured together.

*Drainage and closure.*—Drains were not used as a routine in all cases. If found necessary, a 'cigarette' drain may be introduced extraperitoneally through the loin. Drains were used in only 6 cases. I never used intraperitoneal sulphanilamide in any of these cases. Lastly, the abdomen is closed in layers. I close the peritoneal layer in every abdominal case with a continuous mattress suture, thereby minimizing the possibility of disruption of the abdominal wound. I need hardly mention that perfect asepsis and prevention of soiling of the peritoneum should be maintained from the beginning to the end of the operation. The wound in all cases healed by first intention. There has been no problem of wound infection.

### Post-operative course and complications

*Temperature.*—An absolutely normal temperature was observed throughout in 15 cases. A slight rise of temperature up to 101 degrees was recorded for 3 days in 12 cases, and the rest of the period was afebrile. A moderate daily rise of temperature from 99 degrees to 101 degrees continued throughout the period in 10 cases. One case had diarrhoea for 3 days which was controlled by astringents. Post-operative distension developed in 7 cases. Mild hiccough troubled one patient only. One patient developed threatened obstruction; later a faecal fistula was formed; *B. coli* cystitis continued for a long time, and at last she succumbed with *B. coli* septicæmia as a terminal complication.

The common complications mentioned in textbooks, such as peritonitis, mesenteric thrombosis, pulmonary embolism and pneumonia, were not observed in this series. Garlock and his associates were worried with cardiac, cardiovascular,



pulmonary and other complications as well as wound infections. These were noticeably absent in my series.

#### *Post-operative treatment*

**Diet.**—Rectal glucose and saline were avoided in these cases although we give them as a routine to other abdominal cases. Liquids by mouth can be given freely, but milk is avoided for the first 3 days. Most of the patients were able to take their regular food on the 9th or 10th day.

Pitressin, prostigmin and acetylcholine were frequently used for post-operative distension, and retention of urine. In persistent cases of abdominal distension, pitressin  $\frac{1}{2}$  c.cm. given intravenously is very effective. Post-operative transfusion and ultra-violet ray to tuberculosis patients do much good.

#### *Discussion and conclusions*

Even though the two-stage operation produced no mortality and the one-stage operation produced two deaths, I am convinced that it is far better to resect the colon in one stage rather than in two stages (for reasons stated earlier in this paper) except in patients whose general condition is very poor. Opening the abdomen for the first stage of the operation with a double object in view, namely, to perform ileocolostomy and to develop a separate compartment by the adhesions of the omentum to the sear of the first incision (as advocated by Pemberton and Whittaker, 1937), seems to me quite unreliable. Such a result may not always be obtained. This has been my experience. On the other hand, I have observed that on opening the abdomen for the second-stage operation, much difficulty is encountered in mobilizing the colon and the mesentery, due to adhesions and induration of the tissues. Therefore, I strongly advocate the one-stage operation, even though there were no deaths by the two-stage operation in my series, as the technique described above brings down the mortality rate, and there is no advantage in opening the abdomen twice. In malignancy, where time and reduced intra-peritoneal manipulations are very important, it is advisable to complete the resection in one stage.

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## CLINICAL OBSERVATIONS ON MALARIA CASES WITH DANGEROUS CEREBRAL MANIFESTATIONS

By H. J. HAMBURGER, M.D.

CORRECT diagnosis and immediate treatment are the indispensable requirements of success in attending malaria cases with dangerous cerebral manifestations.

Every observant physician will have learned often through tragic developments, how malaria cases with what appears at first to be the 'usual' attack slide into delirium, or over-night from an apparently healthy sleep into deep coma; or how viciously a pernicious malaria infection may hide itself behind a very varied clinical picture resembling a score of different conditions of almost any organ or system of the body. Cerebral malaria has been diagnosed as cerebro-spinal meningitis; and in this journal only recently attention has been drawn to the fact that even the function and structure of the kidney may be deeply affected, an organ which had so far only to a small extent attracted the interest of malaria workers.

This protean character of malaria becomes understandable if we regard malaria from the pathologico-anatomical aspect as a vascular disease with an ubiquitous distribution of the morbid agent. This very aspect, which makes the situation clear to the pathologist, means for the attending physician, who is called upon to diagnose rapidly and to administer optimal treatment, the necessity of finding his way amongst a welter of often contradictory and surprising clinical signs and symptoms. He therefore is continually searching for gauges and standards by which to assess his findings. It is in this sense that the following 6 cases were compared and an attempt was made to abstract certain salient points from their clinical history. Amongst more than 500 cases of malaria that have come under observation as indoor patients since the beginning of the 1942 autumnal outbreak, the mercifully low number of 6 manifested the pernicious characters that are to be discussed.

#### *Case histories*

Case 1.—A. B., female, 54 years. Admitted with a history of severe attacks every year. Seven years ago

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she had an attack of blackwater fever (?) when she was for several days unconscious. The last attack was about 2 months ago when she had quinaerine and præquine, followed by iron tonic. The immediate history was fever for 36 hours, beginning just as other attacks of malaria; but she got more drowsy than usual and would not take fluids. On admission temperature was 102°F., pulse 100, dry, furred tongue, slight tendency to stiff neck, drowsy, but responding to questions, no other abnormalities detected. Spleen not palpable. Blood in thick drop and film negative for malaria parasites. She could however be roused enough to take fluids and quinaerine 4-hourly. The next morning the condition had much deteriorated, as she had ceased to take fluids during the night. She was nearly unconscious and the stiff neck was more marked. Temperature 102°F. Urine showed now a trace of sugar, albumin plus, an occasional granular cast and very few leucocytes. During the night the temperature had been up to 104°F. for a short while. Diagnosis of cerebral malaria was now made. Lumbar puncture showed the CSF under slightly increased pressure, but clear without any further pathological elements. Intensive quinine and atabrin musonate injection treatment was started. By evening, temperature had come down to 100°F., in repeated blood slides some MT rings having been found. But the cerebral condition had not improved.

Next morning, that is the 4th day of sickness, temperature was 101°F., to remain there for the next 72 hours, i.e. till the fatal end. Facial oedema; urine findings same, but more intense than before. She had during the preceding day and the night some clear moments, but slid again in spite of the most intensive treatment, specific and supporting, into coma interrupted by convulsions, till death supervened.

**Case 2.**—C. D., male, 48 years. Admitted at noon with a history of fever since same morning. No history of malaria. There is, however, a history of heavy alcohol abuse. On admission temperature 102°F., pulse 112, dry, furred tongue, congested throat, cold extremities and nose, tendency to stiff neck, drowsy and only with difficulty to be induced to answer questions. Spleen not palpable. M.T. rings found.

Quinine-quinaerine treatment was instituted at once in four-hour intervals.

Next morning he had not improved, temperature having been up to 105°F., was then around 102°F., stationary all through the day. Drowsiness was more marked, interrupted by short periods of restlessness and complete disorientation.

Reflexes exaggerated, blood pressure 190/110, in urine much albumin, but no formed elements.

The picture presented was now in certain aspects so much like that of case 1, that intravenous quinine therapy was resorted to, besides other supporting treatment, infusions, etc. There was no earlier history suggesting uræmia.

The temperature came down during four days in a lytic curve, in which period urine and blood pressure also were gradually normalized. But the mental and nervous condition remained disturbed for full 10 days, in the character of a serious delusion of the Korsakoff type. Thereafter, under appropriate high caloric, high vitamin diet and sedatives, uneventful recovery.

**Case 3.**—E. F., male, 25 years. A history of fever and gradual onset of unconsciousness interrupted by attacks of tonic and clonic convulsions, for 4 days. Malaria history of irregular attacks of intermittent fever for the last 8 weeks. Had no treatment at all.

On admission temperature of 101°F., which never changed throughout the 12 hours of observation. Pulse weak and very fast. Spleen not palpable, stiffness marked, patellar and achillis tendon reflexes absent, anisocoria of the irregular shaped pupils, no reaction to light. The deeply unconscious patient was from time to time shaken by a series of generalized convulsions. In thick drop, M.T. rings. In urine, albumin plus.

Intravenous quinine and supportive as well as sedative treatments were instituted at once. In spite of

all attempts at treatment, death occurred within 12 hours.

**Case 4.**—G. H., male, 28 years. A history of fever and gradual refusal of fluid intake and supervening unconsciousness interrupted by attacks of violent convulsions, of 3 days' duration. Malaria history of 4 months' recurring attacks, casually treated with quinine.

On admission temperature was 100.6°F., pulse 100, of poor quality and became imperceptible during convulsions. Dry, thickly furred tongue, well marked stiff neck, no tendon reflexes but marked Babinski both sides. Pupils mydriatic, reacting promptly to light. A concomitant squint, which was usually present in him, was much exaggerated. Deeply unconscious, with periods of general convulsions. Spleen not palpable.

In the urine a trace of sugar; a white cell count showed a shift to the left in the leucocytes, total WBC 10,000. The CSF was decreased in pressure, turbid, with 1,600/3 cells, almost all leucocytes. No bacteria could be demonstrated in the fluid, in spite of intensive search with all available staining procedures. Culture was unfortunately not possible. No malaria parasites found. Though the clinical picture and the laboratory findings were equivocal, a diagnosis of cerebral malaria was made, and intravenous quinine treatment started at once. In spite of this he seemed to slide during the night into deep coma. However, under continued intravenous therapy and infusions he had somewhat improved next morning and took some fluid. For 4 days he continued between deep unconsciousness and half-wakedness, whilst the temperature remained fixed around 101°F. Quinine therapy was all the time continued. He finally recovered. The leucocyte count dropped to 4,000, and the nervous symptoms abated. The stiff neck was very slow in disappearing. Recovery was exceedingly protracted. On the 10th day an effusion in the right knee was found. This again made the diagnosis of malaria appear doubtful, but the effusion was sterile on two occasions when each time about 80 c.cm. were withdrawn. It contained a number of leucocytes. In the 6th week the patient was discharged, completely restored.

**Case 5.**—I. J., male, 29 years. A history of having been 'off colour' since the morning and having vomited blood before being brought to hospital.

His history showed that he had had 3 attacks within the last 6 months, all thoroughly treated with quinaerine and præquine, etc. He was moreover known to suffer from duodenal ulcer.

On admission at noon temperature of 100.6°F., pulse almost imperceptible. Unconscious, slightly stiff neck. Spleen not palpable. Very slight increased muscular resistance in epigastric region. Repeated hamatemesis. In the blood M.T. rings and gametes numerous.

A diagnosis of cerebral malaria with bleeding peptic ulcer was made. Under intravenous quinine and calcium treatment he regained consciousness within 2 hours, and had thereafter an uneventful recovery from malaria, and the acute disturbances caused by the (later radiologically confirmed) duodenal ulcer.

**Case 6.**—K. L., male, 50 years. Admitted in a condition of extreme excitement, shouting indecencies, biting and hitting wildly about. He recognized for a few seconds his surroundings, but for most of the time was completely deluded. He presented thus the picture of a maniacal psychosis, and had finally to be strapped, morphia and ice applications being employed. When seen by me he was found to have a temperature of 104°F., a slight rigidity of the neck, a trace of albumin in the urine. Spleen was not palpable. Quinine was at once administered intravenously. Within 1½ hours he recovered completely from his delusion. The next morning the spleen was palpable, and parasites (rings) had meanwhile been found. Uneventful recovery.

### Discussion

It is only reasonable that some doubts should be put forward about the justification of the diagnosis of malaria in all cases. Especially case 1,

but also others have traits suggestive of encephalitis epidemica. However, no epidemiological data support this, and there is an abundance of malarial antecedents. With this approach to precise diagnosis one has to be satisfied, as the object of this note is to which of the possible ways has been chosen to solve a clinical emergency. Case 4 might have been cerebro-spinal meningitis. The knee effusion is most suggestive in that direction, but the complete absence of coeci in the CSF and withdrawn effusion, the response to intravenous quinine and the marked malaria antecedents together with low WBC counts make actually malaria the more likely label. During the first appearance of the effusion high doses of 'daganan' were actually exhibited for two days without any appreciable effect. The appearance of a sterile inflammatory joint effusion as a sequel to malaria is, as far as available literature shows, exceedingly rare.

It may not appear justified to call cases 2 and 5 'cerebral' malaria. Case 2 may have been a Korsakoff psychosis of alcoholic origin precipitated by a malaria infection. It appears very difficult, and perhaps not even worth while, to attempt with the help of the available data to limit what in the clinical picture was due to the 'ubiquitous distribution of the capillary blocks caused by parasites in the brain' and what was the result of chronic degenerative changes of function and/or tissue through alcohol. In case 5 it would be possible to argue that the unconsciousness was the result of collapse from loss of blood.

Of these 6 cases, 4 had malaria. Two cases show how serious results a neglect to seek adequate treatment in time may have. But cases 1 and 5 show that, even if employed, it is not always an absolute safeguard against serious relapse. That alcoholism does not increase the resistance of the patient against a heavy infection will surprise no one. Case 6 demonstrates that even in fresh and uncomplicated cases these cerebral manifestations may appear in an unpredictable way.

Of the clinical findings I wish to emphasize that marked neurological abnormalities, such as stiff neck or upset pupillary function, should not deter one from the correct therapeutic action. Sugar or albumin in the urine is a sign of imminent danger. The absence of splenic enlargement in cases as serious as these may be interpreted as indicating a weakness of the defence system, which may in itself be a causative element of importance. A fixed temperature around 101°F. seems to point to affection of the heat centre possibly due to the anoxæmia caused by the blockage of parasite-filled capillaries. It is at any rate a sign of further danger.

As regards treatment, it was disappointing to see that case 1 ended fatally in spite of vigorous treatment; cases 2, 5 and 6 received adequate quinine and fluid treatment within 24 hours; case 4 recovered in spite of serious delay, case 3 was beyond repair when seen.

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## SOME STATISTICS REGARDING CONFINEMENTS AMONGST 2,500 FULL-TERM PRIMIPARÆ

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and

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THIS work has been undertaken by us with a view to ascertaining amongst the South Indian primiparæ, (1) the percentage of confinements amongst different age groups, (2) the average

(Continued from previous column)

In concluding it must not be omitted to say that infusion therapy should be handled carefully. Our knowledge on the water balance in these conditions is not perfect. It is, for instance, not certain if the brain is in a state of œdema or of dehydration. At present it seems safer to use a slow rectal saline-glucose infusion (Murphy drip) rather than an intravenous saline however slowly and considerately given. For convulsive cases hypertonic glucose solutions should be used.

Finally one cannot evade the question why certain cases develop a pernicious character whilst others remain more or less amenable to the efforts of natural defence and/or treatment. Since all our cases were observed in one locality and season, differences of virulence of the particular parasite strain can be ruled out except perhaps for case 1, which probably was a relapse. The absence of splenic enlargement in our cases, 5 out of 6, cannot be taken at its full face value. Promptly instituted treatment during the primary attack may prevent the splenic enlargement; though the fact that the spleen is not palpable does not prove that important cellular changes in the spleen structure are not actually occurring. However there seems some significance in the frequent absence of splenomegaly in such pernicious cases. Taliaferro and Mulligan (1937) have described how the lymphoid-macrophage system (a wider conception of the reticulo-endothelial system) bears the brunt of defence in malaria. If the spleen does not enlarge in severe infections, one can perhaps deduct from that a failure of the lymphoid-macrophage system to produce the necessary hyperplastic reaction. A discussion of the reason for that would involve immunological and histo-pathological details outside the scope of this note.

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*Confinements at different age groups**Presentations at different age groups*

Age	Total number of cases	Percentage	Cephalic	Breech	Transverse	Total
14-15 years ..	165	6.6	162	2	1	165
16-18 " ..	921	36.8	904	16	1	921
19-25 " ..	1,276	51.0	1,245	28	3	1,276
26 years and above ..	138	5.5	134	3	1	138
<b>TOTAL</b> ..	<b>2,500</b>	<b>..</b>	<b>2,445</b>	<b>49</b>	<b>6</b>	<b>2,500</b>
Percentage ..	..	..	97.8	1.96	0.24	..
Average age ..	19 years	..	..	..	..	..

*Methods of delivery at different age groups and percentage of abnormality*

Age	Total number of cases	Normal labour	Forceps	Internal podalic version	Cæsarean section	Total abnormal labours	Percentage of abnormalities	Average abnormality
14-15 years ..	165	157	6	1	1	8	5	
16-18 " ..	921	855	60	4	2	66	7	
19-25 " ..	1,276	1,161	104	5	6	115	9	
26 years and above ..	138	100	36	..	2	38	27.5	
<b>TOTAL</b> ..	<b>2,500</b>	<b>2,273</b>	<b>206</b>	<b>10</b>	<b>11</b>	<b>227</b>	<b>..</b>	<b>9%</b>

Maternal deaths .. : 19.0  
 Maternal mortality, per thousand .. : 7.6

age at the time of confinement, (3) presentations and methods of delivery at different age groups, (4) the percentage of abnormalities, (5) maternal mortality, (6) average external pelvic measurements, (7) the ratio of births between the sexes, (8) average weight of new-born infant and neonatal mortality.

For the purpose of this inquiry the case sheets of all full-term primiparae confined in this hospital during the last few years have been scrutinized. Only those sheets with full and complete particulars to the number of 2,500 have been selected. The results of this investigation are given in the tables which are given here.

*Average external pelvic measurements*

Inter-spinous ..	8½"
Inter-crestal ..	9½"
External conjugate ..	7"

*Regarding sex, weight and neonatal mortality rate*

Number of cases	Boys	Girls	Alive	Dead	Average weight of infant at birth
2,500	1,305	1,195	2,392	108	6 pounds 2 ounces.
Per thousand	522	478	957	43	

We are grateful to Colonel J. C. Pyper, O.B.E., I.M.S., for encouraging us to do this interesting though laborious research, and to Dr. Ramgopal and Sister L. D'Souza, for helping us with the statistics.

**SULPHAPYRIDINE ANURIA**

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and

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THE renal complications of the sulphonamide group of drugs have received much attention during the last few years, and the literature upon the subject is now extensive. Very little, however, has been published in this country where theoretically, owing to the excessive loss of body fluids by sweating and the peculiar local prejudice against drinking water during fevers, the condition should be more common than in temperate climates.

Since the end of 1938, we have treated over 1,800 cases of lobar pneumonia (apart from many other bacterial diseases) with sulphapyridine, and we have seen a fair number of cases of microscopical hæmaturia, eight cases of frank hæmaturia and two cases of anuria. The incidence of severe renal complications

(0.5 per cent) is therefore low, in spite of the fact that many of our patients are very toxic and dehydrated on admission, and alkalies are not given as a routine. This may be offset by our practice of discontinuing the drug twenty-four to thirty-six hours after the temperature has fallen to normal, and our insistence upon the intake of large amounts of fluid.

Macroscopical hæmaturia, in the eight cases referred to, ceased after withdrawal of the drug and the administration of large quantities of fluid and alkalies. The two cases of anuria, one of seventy-two hours' duration and the other of twelve-hours', responded satisfactorily to treatment, and are worth recording as confirmatory evidence of the value of the accepted lines of treatment.

### Case reports

*Case 1.*—An Anglo-Indian male, aged 64, was admitted into the Kolar Gold Field Hospital on 21st February, 1942, complaining of sudden onset of pain in the left chest, which began a few hours previously. He was orthopnoic, temperature 103.8°F., pulse 120; respiration 36. There were signs of consolidation at both lung bases. Sulphapyridine 9 gm. was given during the first twenty-four hours (tabs. iii 4-hourly) and 3 gm. during the second twenty-four hours (tabs. i 4-hourly). He was afebrile twenty-four hours after admission and the drug was stopped after forty-eight hours when a total of 12 gm. had been given. Urine examination on admission revealed a slight trace of albumin, with a few leucocytes in the deposit.

At 1-30. p.m. on 23rd February, i.e. four hours after the drug had been stopped, he complained of severe lower abdominal pain and burning in the testicles. There was no pain in the loins. The urine was smoky, reaction acid, and there was a heavy cloud of albumin with numerous red blood cells. Fluids were pressed and sodium bicarbonate and potassium citrate given by mouth. A small quantity of bloody urine was passed on the morning of 24th February. The fluid intake on 25th and 26th February was 78 and 77 oz. respectively, but there was complete anuria. On 26th February the blood urea was 202 mg. per 100 c.cm. To promote diuresis, 300 c.cm. of 4.28 per cent sodium sulphate in triple distilled sterile water were given by intravenous drip. One hour later the patient had a sudden attack of dyspnoea and cyanosis which was relieved by giving 1.7 c.cm. of nikethamide subcutaneously, and intranasal oxygen. The blood pressure was then 160/105. It should be noted that the triple distilled sterile water used in this case was used in other cases without any abnormal reactions.

On 27th February (after seventy-two hours' anuria) cystoscopy was performed by one of us (G. E. D.) under spinal anaesthesia. There was no fluid in the bladder on preliminary catheterization, but a few small blood clots were washed out during irrigation. The left ureter was catheterized and clear dilute urine immediately dripped from the ureteric catheter and continued throughout the procedure. The

ureter was then irrigated carefully with 15 c.cm. of normal saline. The right ureteric catheter was passed only half an inch when it met with a resistance. Ten c.cm. saline were injected into the catheter and could be seen issuing from the ureteric orifice beside the catheter, but all attempts to pass the catheter on this side failed. The left ureteric catheter was left *in situ* for several hours.

The following table shows the blood urea findings, fluid intake and quantity of urine passed during the next five days:—

	27th February	28th February	1st March	2nd March	3rd March
Blood urea, mgm. per cent.	138	218	..	..	42
Fluid intake, oz. ..	75	118	103	99	117
Urine passed, oz. ..	90	125	65	40	72

Pain persisted until 3rd March, and microscopical hæmaturia until 15th March, suggesting that the deposit in the right ureter remained for some days. On 23rd March, intravenous pyelography showed no evidence of obstruction in either ureter and the patient was discharged on 25th March.

*Case 2.*—A Mohammedan male, aged 42, was admitted into the Kolar Gold Field Hospital, on 26th October, 1942, complaining of cough and right chest pain of two days' duration. Temperature 102.4°F., pulse 120, respiration 30, general condition fair with moderate dehydration and consolidation of right lower lobe. The urine was amphoteric with a slight cloud of albumin and a few red blood cells and leucocytes. He was given sulphapyridine tabs. ii (1 gm.) 4-hourly for forty-eight hours followed by tab. i (0.5 gm.) 4-hourly for twenty-four hours. Total 30 tablets (15 gm.) in seventy-two hours. There was a permanent fall in temperature with disappearance of toxæmia in thirty-six hours.

A few hours after the sulphapyridine was stopped the patient complained of pain in both loins and hypogastrium, and inability to pass urine. On catheterization the bladder was found to be empty. The blood urea was 30 mgm. per cent. Intravenous drip saline with 6 per cent glucose was commenced, and soon after 2 oz. of highly blood-stained urine were passed. The anuria had lasted for twelve hours. Parenteral saline was continued for thirty-six hours until 5 pints had been given, and in addition fluids were pressed orally. The dehydration rapidly improved and a satisfactory diuresis was established. Macroscopical blood disappeared by the next day, but red blood cells were found in the urine for a further period of three days.

### Comment

Renal complications during sulphonamide therapy vary from microscopical hæmaturia to



complete anuria, and are due to the deposit of the insoluble acetyl salts of the sulphonamides in the kidney tubules and ureters. Margolin (1941) has shown that in an acid medium, the acetyl salts of sulphapyridine and sulphathiazole are precipitated as insoluble long and sharp crystals. The lower third of the ureter and particularly the entrance to the bladder are the principle sites of obstruction (Stryker, 1940).

It is now well established that hæmaturia, oliguria and anuria complicating sulphapyridine therapy can generally be avoided by giving more than 5 pints of fluids daily. This large intake is necessary to produce an effective flushing out of the kidneys and ureters, and to prevent a high concentration of the relatively insoluble acetyl sulphapyridine. When vomiting interferes with the absorption of a requisite amount of fluids, resort should be had to intravenous administration, whilst the sulphapyridine therapy is continued by intramuscular injection of its soluble salt. An additional safeguard is stated to be alkalization of the urine, for it has been shown that acetyl sulphapyridine crystals are less frequently deposited in alkaline urine. Fox *et al.* (1943), however, express their opinion that the solubility of these crystals is not sufficiently increased, even in highly alkaline urine, to prevent precipitation.

Kawaichi and Barnes (1941) suggest that severe cases of hæmaturia can be avoided by daily microscopical examination of the urine. We consider this impracticable especially in this country; in addition the presence of a few red blood cells in the urine in highly toxæmic patients is not unusual even when chemotherapy is not used (*vide* case 2), and need not be attributed to sulphapyridine. It is surely simpler to insist on an adequate fluid intake, and naked eye inspection of all specimens of urine. When gross hæmaturia occurs, the drug should be stopped, the fluid intake further increased, and the urinary output measured. Almost all cases will respond to this treatment.

If the urinary output continues to fall, intravenous saline and glucose should be given immediately, and intensive alkalization instituted. In many cases of oliguria and early anuria this is sufficient to produce a satisfactory diuresis (case 2). If this treatment is ineffective and anuria occurs, a relatively simple procedure described by Flynn (1943) is worth trying. Flynn has successfully treated eight cases of sulphapyridine anuria by massage of the lower end of the ureters per rectum combined with massage over the kidney regions. Rogan and Cruickshank (1942) describe a case in which inductotherm (short wave) treatment to the kidney region resulted in a cure.

If these measures fail, cystoscopy and ureteric catheterization should be performed. Our unpleasant experience with intravenous sodium sulphate questions the advisability of its use. Case 1 demonstrates that the patient's general condition may remain apparently good

for several days after the onset of anuria. This is unfortunate, as procrastination may lead to a fatal outcome. It is worth emphasizing that difficulty may be experienced in passing the ureteric catheter, firstly, because the ureteric orifice may be obscured by collections of deposit, and secondly, the lower third of the ureter may be blocked. The latter condition was found in case 1 and is also referred to by Kerr (1943) and Flynn (1943). In our case, catheterization of the left ureter was immediately followed by the passage of clear urine, and at first gave the impression that the operation had coincided with a natural cure, but the complete inability to catheterize the right uréter revealed the ominous nature of the condition.

As a last resort, if all attempts at ureteric catheterization fail, or in children when the technical difficulties may be insurmountable, it is legitimate to perform a pyelonephrostomy as recommended by Tsao *et al.* (1939) and De Lacey, Cohen and Spencer (1943). If this operation fails, it may be assumed that the renal tubules are completely obstructed.

### Summary

1. Two cases of sulphapyridine anuria are described. One was of seventy-two hours' duration and the other of twelve hours'. Re-establishment of the urinary outflow was achieved in the first case by ureteric catheterization, and in the second by intravenous saline and glucose.

2. A short outline of the treatment of the condition is given.

### Acknowledgment

We wish to express our thanks to Messrs. John Taylor & Sons, Managers of the Kolar Gold Field, for permission for publication.

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# EFFECT OF YEAST AND YEAST PRODUCTS ON COMPLEMENT OF GUINEA-PIG SERUM

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*Defects in guinea-pig serum in Calcutta.*—The senior writer (S. D. S. G.) found in 1934–36 that in Calcutta, for the major part of the year, the complement of guinea-pig serum did not work with the Wassermann antigen prepared according to the method of McIntosh and Fields. This antigen is one of the standard antigens recommended by the Medical Research Committee

(British, now Council, 1918) and is probably used more than any other in India.

When the animals felt the discomfort of the climate, two defects appeared in the complement: (i) it lost its titre, and (ii) later, it became 'cholesterol-shy' (Greval, Chandra and Das, 1940). Of such a complement more than the usual allowance was required in its titration in the presence of the antigen for the correspondence between the two rows of tubes (front row without and back row with the antigen). That the animals were not suffering from epizootics at these periods was shown by an absence of increase in mortality.

The titre could be restored by providing more comfort, such as ice in the animal house in the hot weather, and warmth and more food in the cold weather. The cholesterol shyness remained.

*The defects removed by marmite.*—It was also noticed that the animals tended to grow bigger than usual. Some defects allied to nutritional oedema and beri-beri were suspected and the animals were put on marmite (four

*Selections from the record of titration of complement for June to September 1941 and 1943*

	FIRST ROW, WITHOUT ANTIGEN (ONE VOLUME OF DILUTION IN EACH TUBE) Dilution of 1 in :—								BACK ROW, WITH ANTIGEN (TWO VOLUMES OF DILUTION IN EACH TUBE) Dilution of 1 in :—							
	20	30	40	50	60	70	80	90	20	30	40	50	60	70	80	90
In 1941																
1. Best batch (2-7-41)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
2. Worst batch (16-7-41).	—	—	±	±	+	+	+	+	—	—	—	*—	±	±	T	+
In 1943																
3. Best batch before treatment with yeast (2-7-43).	—	—	—	—	±	+	+	+	—	—	—	—	T	+	+	+
4. Worst batch before treatment with yeast (7-7-43).	—	—	?—	±	+	+	+	+	+	+	+	+	+	+	+	+
5. Best batch after treatment with yeast (2-9-43).	—	—	—	—	?—	±	+	+	—	—	—	—	±	+	+	+
6. Worst batch after treatment with yeast (6-8-43).	—	—	—	±	+	+	+	+	T	T	+	+	+	+	+	+
7. Best batch after one week's treatment with vegemite (26-8-43).	—	—	?—	±	+	+	+	+	—	—	±	+	+	+	+	+
8. Worst batch after one week's treatment with vegemite (24-8-43).	—	—	—	—	—	—	—	?—	—	—	±	+	+	+	+	+
9. Best batch within two weeks of stopping vegemite and re-administering yeast (7-9-43).	—	—	—	—	?—	±	+	+	—	—	—	—	T	+	+	+
10. Worst batch within two weeks of stopping vegemite and re-administering of yeast (6-9-43).	—	—	—	—	?—	±	+	+	±	?—	±	T	+	+	+	+

— Complete lysis of rbc.

+ Complete inhibition of lysis.

T Trace of lysis.

Combination and modification are self-explanatory.

\* An instance of 'cholesterol-fast' complement.

teaspoonsful a day for 100 animals for the first few weeks, then two teaspoonsful daily). Both the defects disappeared within two weeks and, with the addition of marmite to the food, did not appear again for five years.

This year (May 1943) the senior writer on his return from military duty after an absence of nearly two years encountered the same defects again. The marmite had been unobtainable for six months or so.

**Yeast tablets and vegemite.**—Tablets of yeast were administered (8 tablets of  $6\frac{1}{2}$  grains each a day for 100 animals). Some improvement was noticed in two weeks. The dose was increased to 12 tablets. The improvement continued; but after six weeks of treatment the complement was still on the shy side.

A small supply of vegemite now became available. Half the animals were put on it (four teaspoonsful a day for 100 animals instead of the yeast). A complement of optimal titre and reaction with cholesterol was obtained on the fifth day of the treatment.

The next week, the batch of animals which had not received vegemite was bled. The complement from this batch too was nearly normal.

(The animals are divided into ten batches and marked: The batches are bled from the heart, in rotation, on five days a week. Each batch is thus bled on the same day of the week after fourteen days' rest. A holiday adds an extra fortnight of rest. Dead animals are replaced from the stock.)

The supply of the vegemite only lasted fourteen days.

The accompanying table gives selections from the record of the titration of the complement for June to September 1941 and for the same period this year, without and with treatment.

Overdosing with marmite was likely to make the complement 'cholesterol-fast' (Greval, Chandra and Das, 1940). Of such a complement, less than the usual allowance was required in its titration in the presence of the antigen. This fault in the opposite direction is shown in the table of titrations, from the record of 1941.

For the Wassermann reaction, in the complement-antigen system for the cholesterol-shy and cholesterol-fast complement, and for the complement which is not of optimal titre, adjustments can be and are being made. The complement of optimal reaction and titre is, however, indispensable for standardizing the reagents and for complement fixation tests in kala-azar (Greval, Sen Gupta and Napier, 1939), leprosy (Greval, Lowe and Bose, 1939) and hydatid disease (Greval, Chandra and Das, 1941) which are linked to the Wassermann reaction in this laboratory.

Unlike vitamin C, vitamin B has not been associated with the complement product by other workers.

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## REPORT ON THE OCCURRENCE OF NAGA SORE IN CALCUTTA

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and

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NAGA SORE or *ulcus tropicum* has never been reported from Calcutta or its surrounding places. Its endemicity in the adjoining province of Assam is well known, but Calcutta and its surrounding districts of Bengal had always been free. Since July 1943 many cases of Naga sore have been coming for treatment in the Skin Clinic of this Institution, and on inquiry we found that these were not imported cases from Assam but occurred locally in Calcutta and its suburbs. Careful inquiry elicited the fact that this sore had been present in and around this city in epidemic form during the recent monsoon months, and many hundred cases could be detected. Two cases reported here came towards the end of July, twelve cases in August, twenty-six cases in September, sixteen cases in October and thirteen cases in November 1943. The epidemic is confined almost entirely to the destitute famine-stricken people of which the city and the suburbs have recently been full.

The sudden epidemic of the disease is certainly due to the extreme debility, extreme unhygienic conditions and extreme overcrowding of these poor famished people. These people have been living in the open streets of the city, crowded together, and have to stand for long hours in queues to get some food. At night they have crowded together on the pavements of the streets. Flies and mosquitoes are prevalent in the city and these insects, probably the flies, may have been responsible for the dissemination of the disease, as the lower extremities below the knee joints are mostly affected. The original source

(Continued from previous column)

### Summary

1. For the major part of the year, guinea-pigs in Calcutta yield a serum which is defective for complement fixation tests including the Wassermann test.

2. The administration of marmite, yeast tablets and vegemite removes the defects.

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of the infection is presumably from some of the imported cases amongst the evacuees from Assam, and the disease spread rapidly in epidemic form under the favourable conditions, i.e. the monsoon season, debility due to starvation, overcrowding and dirt in these homeless and famine-stricken people.

As the condition is new in this part of the country, a short description of the disease and its treatment will not be out of place here.

*Synonym.*—Ulcus tropicum, Cachar Sore, Jungli ghao, Phagedænic ulcer, Frontier Sore.

*Geographical distribution.*—It is widely distributed in the tropical and sub-tropical regions: Egypt, Abyssinia, Sudan, Zanzibar, Indo-China, Straits Settlements, Southern China, Malay States, East Indies, West Indies.

In India the disease occurs in endemic form in Assam. It has never been reported from Calcutta and its neighbouring districts. This is the first time it has occurred here and spread in an epidemic form.

### *Ætiology*

*Age.*—It occurs at any age, but is commonly found in adults because of their work in the jungle and in the gardens.

*Sex.*—Both sexes are affected, but the incidence in the males is higher, presumably because of their outdoor work.

*Seasonal influence.*—It is endemic in the tea gardens and jungles in Assam, and becomes epidemic in the monsoon months from May to September, reaching the maximum in the months of July and August, and then gradually diminishing with the advent of cold weather.

*General considerations.*—It is normally confined mostly amongst poor people working in the jungle, the hill tribes and labourers in the field and in the tea gardens. Poverty, debility and unhygienic surroundings appear to play an important part. The condition affects mostly the lower extremities below the knee, parts which are usually uncovered in the labouring classes and are subjected to injury and insect-bites; these factors probably have a bearing on the causation of the disease.

*Causative organisms.*—Bacteriological examination of the smear from the sloughs, the base of the ulcer and the discharge, show an abundance of gram-positive rod-shaped bacilli tapering at both ends—the fusiform bacilli, and a few long slender spirochætes (Vincent's spirochætes). The fusiform bacilli are always present in abundance even in the micro-section. The constant presence of these organisms in large numbers in all the cases of this series is presumptive evidence of their being the cause of this disease. In a few cases, common pyogenic organisms were found in small numbers in addition to the fusiform bacilli, but these are not constant nor in sufficient numbers to suggest that they may cause the condition.

Spirochætes were also present along with the fusiform bacilli in most cases, but they were

not constant and were few in number in comparison with the fusiform bacilli. In the smear from the scrapings from the base of the sore after thorough removal and cleaning of the slough, the fusiform bacilli were often so numerous that the smear appeared to have been made from a culture of the fusiform bacilli.

Inoculation under the skin of the pus or of the discharge from the ulcer produces a typical sore in seven days.

There has been much discussion as to the organisms responsible for this disease, and various authors have incriminated various micro-organisms. Castellani, Manson, Scheube and others attribute this condition to the infection by fusiform bacilli, others to the spirochætes and some others to gram-positive diplococci.

*History.*—There is usually a history of trauma or insect bite with a cut or abrasion of the skin surface. This very soon becomes septic and a small ulcer is formed covered with a greyish yellow slough. The ulcer then spreads rapidly and in a week's time assumes the typical shape and form and may be half to one inch in diameter.

*Description.*—It is a rapidly spreading ulcer, round, oval or irregular in shape and of various sizes depending on the duration of the disease. The most characteristic feature of the ulcer is a thick greyish yellow purulent slough filling the entire ulcer cavity. The slough is loosely adherent and very foul smelling. There is a thin sero-sanguinous putrid discharge from the ulcer. The edges are raised and the ulcer is undermined and deep. When the slough is removed, a raw granulating surface is left which easily bleeds. The ulcer is quite deep and easily reaches the deep fascia where it is usually arrested but may reach even deeper down to the bones. In size it may attain several inches in diameter, and ulcers of 2, 3 or 4 inches in diameter are common. Ulcers may be single or multiple, and may affect one or both the legs. The tissues surrounding the ulcer may be normal, or else slightly oedematous and red. In the early stages, when the ulcer is spreading rapidly, there is some oedema and redness round the margins, but in old cases the surrounding tissues are usually normal. The neighbouring lymphatic glands are not involved.

*Distribution.*—The commonest site is the lower part of the legs below the knee. The thighs are less affected and the upper extremities and the trunk are affected but rarely. In our series of forty cases, only one case had an ulcer on the elbow. In Roy's (1928) series in Assam, out of 386 cases, two were in the upper extremities, and two were in the trunk and, in the remaining 382 cases, the legs and feet were affected.

*Symptoms.*—Although pain is often complained of and is sometimes acute, it is much less than one would expect from such extensive sloughing lesions. It is not a constant feature, but enquiry will usually elicit this complaint.

Fever is as a rule present only when there are multiple lesions, and is apparently due to the absorption of toxins from large septic areas; it soon disappears when the patient is put to bed and the slough is cleaned.

**Treatment.**—There is as yet no specific remedy, and the treatment is mostly symptomatic. In a hospital in which individual attention is possible, the patient should be put to bed and given a liberal diet. Rest and good food are of great help in shortening the duration of the condition. The slough should be loosened and then removed by the application of hydrogen peroxide, followed by a bath of Condy's fluid (1 to 5,000) for half an hour every day, and then by a normal saline compress every hour by day. At night the ulcer is dusted with equal parts of boric acid and sulphathiazole or sulphanilamide powder, and bandaged up. When the slough is entirely removed and the ulcer looks healthy, dressing twice daily with  $\frac{1}{2}$  per cent aeriflavin ointment is sufficient to promote healing. It usually takes three to six weeks for a complete cure. Quick removal of the slough and the mild antiseptic dressings are the principal factors in treatment.

But the difficulty arises in field treatment in an epidemic in a tea garden or in the Army labour corps when a large number of cases have to be treated as out-patients.

For mass treatment the following methods are recommended.

**I. Modification of McGuire's (1934) treatment.**—The slough is removed forcibly by a cotton swab soaked in copper sulphate and phenol lotion twice every day, and the wound is dusted over with sulphathiazole or sulphanilamide powder alone or with boric acid.

*Copper sulphate and phenol lotion*

Copper sulphate	..	..	2 drachms
Phenol	..	..	1 drachm
Aqua	..	..	1 oz.
(Copper sulphate should be powdered well and dissolved in water first; and the phenol added last.)			

*Dusting powder*

Sulphathiazole or sulphanilamide	..	1 part
Boric acid	..	1 part

**II. (a)** The slough is removed gradually by dressing the sores with desiccated magnesium sulphate powder once daily or with the saturated solution of magnesium sulphate twice daily.

**(b)** As soon as the slough is removed, the ulcer is dressed with gauze soaked in brilliant green and zinc sulphate solution once or twice a day,

Brilliant green	..	..	5 grains
Zinc sulphate	..	..	2 grains
Aqua	..	..	1 oz.

or in triple dye solution.

Aeriflavin	..	..	10 grammes
Brilliant green	..	..	2.5 grammes
Gentian violet	..	..	2.5 grammes
Aqua	..	..	1,000 c.cm.

(Concluded at foot of next column)

## INCREASING INCIDENCE OF *TÆNIA SOLIUM* INFECTION IN CALCUTTA

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THE incidence of *Tænia solium* infection has always been much less than that of *T. saginata* in Calcutta. During the last fifteen years (1928 to 1942) we have come across 281 cases of *T. saginata* infection but only 3 cases of *T. solium* infection amongst the patients either admitted in the Carmichael Hospital for Tropical Diseases or attending the out-patient clinic of this department. The total number of persons examined during this period was 20,664. *T. saginata* infection was found in 281, whilst *T. solium* infection was found in 3 only.

This year (1943) up to the middle of August, we have examined a total of 887 patients in our hospital and out-patient clinic. We have already found 22 cases of *T. saginata* infection and 6 cases of *T. solium* infection. Evidently the incidence of both the infections is rising, but especially that of *T. solium*. This is alarming, in view of the fact that *T. solium* infection is of potential danger to man.

*T. solium* (pork tapeworm) infection is acquired by eating raw or insufficiently cooked pork infected with the *Cysticercus cellulosæ* ('measly pork'). These cysts in pork look like pomegranate seeds, and are popularly called 'Dalim dana'. In the slaughter houses, measly pork is thrown away and is not sold to the public. But during the last three months, we have known of two instances of measly pork being openly sold in the butchers' shops in Calcutta. This is probably due to the heavy demand for pork this year owing to the abnormal increase in the number of people in the city at present.

Hogs get infected with *C. cellulosæ* by eating the faeces of man containing the eggs of *Tænia solium*; hogs reared by firms of repute on clean food are always safe for human consumption. It is only those country hogs which are not cleanly fed that are responsible for this tapeworm in man. Owing to the heavy demand for pork, such unclean country hogs are probably brought to the city and butchered by unauthorized dealers, and the meat is being offered for sale to the ignorant public.

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When the ulcer is superficial and healthy looking, a  $\frac{1}{2}$  per cent aeriflavin ointment dressing applied once daily will complete the treatment.

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## LOCALIZED PRETIBIAL 'MYXCEDEMA' IN THYROTOXICOSIS

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In some cases of thyrotoxicosis, nodular or plaque-like swellings of the pretibial areas are found. These swellings on histologic examination are found to be due to a deposition of mucinous substances in the skin. This condition, as Sir Thomas Dunhill (1935) says, is interesting rather than serious.

There are other types of localized myxœdema not associated with thyrotoxicosis, which are not considered here.

There is no agreement in regard to the nomenclature of this condition. It has been described by many authors by different names: localized myxœdema, localized pretibial myxœdema, mucoid degeneration of the skin in association with hyper-thyroidism, etc. The objection to the term myxœdema is that such a localized pretibial accumulation of mucin

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*T. solium* is of grave danger to man, as, if the eggs are accidentally ingested with water or food, especially unecooked green vegetables contaminated with the eggs, the cysticerci may develop in man. Man harbouring *T. solium* may also get cysticercus infection by auto-infection through unclean personal habits, whereby the eggs reach the mouth, or the gravid segments in the intestine may be regurgitated into stomach; then the eggs hatch and the larvae develop into cysticerci in the tissues. Cysticerci in the brain produce mental and nervous symptoms, especially certain forms of epilepsy which have caused death. Eighty-one cases of cysticercosis (mostly cerebral) have been reported up to 1935 amongst British soldiers stationed in India.

*T. saginata*, or the beef tapeworm, is merely a nuisance and is acquired by eating raw or insufficiently cooked beef containing *Cysticercus bovis*. It does not produce cysticercosis in man and is therefore apparently a harmless parasite.

The 6 cases of *T. solium* infection and their probable sources of infection are enumerated below:—

(1) Englishman, age 46, Government official (pork and sausages). (2) Coolie, age 32 (pork). (3) Anglo-Indian child, age 5, of poor family (sausages). (4) Anglo-Indian child, age 4½, of poor family (sausages). (5) European nun, age 40 (pork and sausages). (6) Anglo-Indian child, age 1½, of well-to-do family (sausages).

**Conclusion.**—As 6 cases of *T. solium* have already been seen up to the middle of August this year (as compared with 3 cases seen within the last fifteen years), it is apprehended that the incidence of *T. solium* is increasing in Calcutta. We desire to draw the attention of the authorities to this fact.

under the skin is not found in myxœdema, but for want of a proper name and in order to facilitate reference to earlier literature, the name has been retained. It has been suggested by Webber (1937) that the word myxœdema should be in inverted commas.

Trotter and Eden (1942) have recently reviewed 73 cases of this condition mentioned in literature, and have recorded 4 cases of their own. The majority of cases have been in Europeans. Two cases were in Negroes and one in a Chinese patient. There is no mention of any similar case in India. In 1939 I came across one case of this condition which I am recording here.

### Case record

Mrs. A. A. H., Mohammedan, aged 30 years, was admitted under the care of Mr. S. J. Mehta, F.R.C.S., for toxic goitre. The swelling in the neck first appeared ten years ago accompanied by pain on swallowing, and fever. She was treated by a local practitioner and was well for two years. Then she gave birth to a child and after delivery she had a recurrence of the swelling and palpitation. Again she was treated and the symptoms subsided. During the last six years she had recurrent attacks of the swelling but the same beneficial effect of treatment was not seen. During the last three years the swelling began to grow rapidly and palpitations became marked. She now complains of excessive sweating, loss of weight and weakness. The loss of weight is marked and, according to the patient, she is half her original weight. She is very nervous and very irritable, and quarrels with her husband. She has lost five children and her irritability is ascribed to this. Her menstrual periods are irregular and flow is scanty.

On examination, she is of average built but thin; weight 56 lb.; height 5 feet. The eyes appear staring, though not very prominent. The other eye signs are absent. There is a big thyroid swelling, firm, vascular and lobulated, measuring 3½ inches by 2 inches by 1½ inches. The veins in the neck are visible; the tonsils are enlarged. She has fine tremors of the fingers and tongue. Her pulse is fast and regular: 145 on admission, 110 to 120 after rest, 84 under basal conditions. It increases very much on the slightest excitement, the pulse recorded by the house surgeon being distinctly higher than that recorded by the nurse. The blood pressure also varies considerably, being 172 mm. of Hg. systolic and 64 mm. of Hg. diastolic after admission, and 130 mm. of Hg. systolic and 68 mm. of Hg. diastolic under basal conditions. The heart is not enlarged; the first sound is accentuated at the mitral area and the second sound at the pulmonary area. There is a systolic murmur best heard in the pulmonary area. It is soft and not conducted. There is also a localized soft systolic murmur at the mitral area. Liver and spleen not palpable. C.N.S.—nothing abnormal detected, except irritability. Her basal metabolic rate is plus 36 per cent. Blood examination showed a moderate degree of hypochromic anemia. Urine showed nothing abnormal.

The curious feature of the case is that both her lower limbs are ungainly due to bilateral diffuse plaque-like swellings extending from below the knees and ending above the ankles. The skin over the swellings is dry. There is no pitting on pressure, but there is tenderness.

The patient was put on Lugol's iodine, and was carefully prepared for operation. The operation was performed under local anaesthesia with a little ether and oxygen intratracheally and paraldehyde per rectum. The patient, however, succumbed a few hours after the operation. She had developed auricular fibrillation. Post mortem was not possible.

**Incidence.**—The condition 'pretibial myxœdema' has not been known to occur by itself or in association with any disease other than

thyrotoxicosis. It is not associated with other disorders of the thyroid gland such as non-toxic goitres or myxœdema. Even in thyrotoxicosis it is not common. In a series of 80 cases of thyroid diseases seen by me, there were 35 cases of non-toxic goitre, 36 cases of toxic goitre, and 9 cases of hypo-thyroidism and myxœdema. Of all these, only one case of toxic goitre showed this condition. In 33 cases of disturbances of glands other than the thyroid, no such case was encountered. Trotter and Eden (1942) give a 3 per cent incidence of localized myxœdema in thyrotoxicosis, and Dunhill (1935) gives the same incidence. This condition is more prone to occur in cases of recurrent or residual thyrotoxicosis. Of the recorded cases, the majority have been of toxic diffuse type. The present case was of the recurrent type, and the goitre was of the nodular type similar to the cases described by Hecht-Eleda (1937), Netherton and Mulvey (1935), and Schwartz and Maddren (1941). In some cases the condition appears after thyroidectomy for thyrotoxicosis, and in some of these cases there were symptoms of hypo-thyroidism.

*Clinical features.*—In the majority of cases there are no special symptoms in the legs. In some cases there was burning and itching, as in 5 out of the 6 cases of Netherton and Mulvey (1935). In others were vague complaints of aching, pricking or tingling sensations. In the present case there was tenderness.

The appearance is characteristic and easily recognizable. The swelling is bilateral and symmetrical. It is strictly limited in the majority of cases below the knees and above the ankles. Rarely it may extend to the toes and up to the knees. The antero-lateral surface of the legs is most involved. There are two main types of the swelling, (1) the nodular type in which the surface is made up of irregular lumps which may coalesce and (2) the continuous plaque type in which there is uniform swelling. The skin shows a characteristic appearance described as 'pig skin', due to the dimpling caused by attachment of hair follicles to their deeper structures. The colour of the skin may be normal or may be pink or brown. The swellings are firm to the feel. There is no pitting on pressure. Usually the skin is dry but normal sweating may be present. In a case mentioned by Bamber (1937) there was excessive growth of hair on the legs.

*Biopsy.*—Glairy fluid is said to exude from the cut surface.

*Histology.*—There is an absence of any sign of inflammation. The most characteristic feature is the splitting apart of the connective fibres of the cutis. There is collagen degeneration in the upper half of the pars reticularis; the collagen bundles are found to be in a loose network—the interstices being filled with mucoid material. In the deeper parts of the corium, there are numerous large phagocytes containing light brown granules of blood pigment.

*Onset.*—According to Trotter and Eden (1942), in 32 cases the swellings appeared before treatment of thyrotoxicosis as in the present case. Two patients developed the condition after treatment and 35 after thyroidectomy for thyrotoxicosis.

*Course.*—The course is very variable. The condition often remains stationary for long periods. The swellings may increase or diminish for no apparent reason. There is no change in this condition produced by the administration of thyroid extract or Lugol's iodine. Dunhill (1935), Langdon-Brown and others report that thyroidectomy is followed by either disappearance or improvement of the condition. In 6 out of the 7 cases of Dunhill, the condition disappeared completely and there has been no recurrence, in one case for as long as 9 years. The Americans, however, state that it re-appears later. Trotter and Eden believe that the lesions tend to disappear spontaneously over a period of a few years.

*Treatment.*—There is no effective treatment.

*Causation.*—There is no agreement regarding its causation. A majority of observers consider it as a manifestation of hypo-thyroidism occurring locally. It must, however, be pointed out that excess of mucin is present in only a small number of cases of hypo-thyroidism and myxœdema.

Myxœdema and thyrotoxicosis are two opposite conditions believed to be due to hypo- and hyper-function of the thyroid gland. The occurrence of these two conditions in one and the same patient would throw doubt on this aetiology. The simultaneous occurrence of opposite conditions in the same patient lends support to the views held by Moebius, Plummer, Boothby and others that the secretion of the thyroid gland is altered in quality, in other words there is dis-thyroidism in thyrotoxicosis and not hyper-thyroidism. When the gland is secreting an abnormal secretion, it is possible that normal secretion may be diminished resulting in myxœdema manifestations. Keining (1928) and Pillsbury and Stokes (1931) also support this view.

According to Trotter and Eden (1942), since mucin accumulation under the skin occurs only in hypo- and hyper-thyroidism, the aetiological agent must be a common one, and they ascribe this rôle to the anterior pituitary gland. In this connection the thyrotrophic hormone is well known. Cope (1938) advances the view that hyper-activity of the anterior pituitary gland is the immediate cause of thyrotoxicosis. This view is steadily gaining ground.

Marine, Rosen and Spark (1935) and Hertz and Oastler (1936) have shown that destruction of the thyroid either by operation or disease is followed by pituitary over-activity. Thus both hypo- and hyper-function of the thyroid gland may be traced to the stimulation of the anterior pituitary.

There is no satisfactory explanation of the confinement of accumulation of mucin to the pretibial area.

### Summary

1. A case of 'localized pretibial myxœdema' associated with thyrotoxicosis has been reported.

2. The clinical features met with in this condition are described.

3. A brief discussion regarding its causation has been included.

My thanks are due to Mr. S. J. Metha, F.R.C.S., for permitting me to investigate this case, and the Superintendent, Sir J. J. Group of Hospitals, for permission to publish the same.

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## A Mirror of Hospital Practice

### A CASE OF ABDOMINO-THORACIC INJURY, PROLAPSE OF OMENTUM; PRIMARY SUTURE OF DIAPHRAGM AND CHEST WALL, RECOVERY

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MAHABIR RAI, 35 years, a clerk, was admitted into the Monghyr Sadar Hospital at 12 noon on 25th April, 1943. He had an open chest wound on the left side with the omentum prolapsing in and out of the wound in the chest wall with each respiratory movement.

The attendants gave the history that he was riding on the top of a bus at about 10-30 a.m. when a protruding bare branch of a tree struck him on the left side of the chest. He was immediately helped down the top of the bus on to the ground when it was noticed that he had a large wound on the left side of his chest and that the 'intestine' was prolapsing through it. He had great difficulty in breathing, and the attendants very wisely tied an improvised bandage round the chest and closed the perforation. Respiration became immediately easier and he was immediately brought over to the hospital on the same bus, this time, more wisely, lying inside the bus.

Examination revealed a very well built, rather obese individual, in moderately severe shock. Dyspnoea was marked and he complained of severe pain in the chest at the site of the wound in his thorax and also in the epigastrium. His respiration rate was 40 per minute, pulse 120, temperature 97°F. There was distinct lividity of the face, lips and finger-nails; thirst was marked,

speech was reduced almost to a whisper and all that he could manage to convey, with extreme difficulty, was that he could not breathe.

He had a lacerated wound 1½ inches by ¾ inch directed obliquely on the antero-lateral aspect of the left side of his chest, with fracture of the 5th and 6th ribs 4 inches from the sternal margin. About 2 inches of the omentum was found prolapsing through the wound and was partly retracted with each inspiratory movement.

There was no surgical emphysema round the wound; percussion of the left side of the chest revealed a hyper-resonant note; breath sounds were indistinct and the cardiac impulse was not felt. There was slight tenderness in the epigastrium and slight guarding but no distinct rigidity or distention.

Morphine gr. ¼ with atropine gr. 1/100 was injected immediately. Intravenous glucose and saline drip was started, and half an hour after admission, a thoracotomy was performed under open ether anaesthesia.

The wound in the chest wall was excised and it was found necessary to enlarge it by 2 inches on either side to enable the thoracic cavity to be fully explored. The damaged portion of the omentum projecting outside the thoracic wound was excised, and the rest returned into the abdomen through the rent in the diaphragm which involved its left leaf and part of the central tendon and was 1 inch by ¾ inch in size. The diaphragm was closed by interrupted catgut sutures. It was found necessary to suspend the manipulations every 3 to 4 minutes, and close the thoracic wound with moist saline packs to minimize the respiratory embarrassment. The pleural cavity was cleared gently with moist swabs. The left lower lobe of the lung was slightly contused but there was no hæmorrhage or laceration and it was left undisturbed. The pericardium was intact and uninjured.

The pleural cavity was securely closed by inserting five pericostal sutures. Soluseptasine 20 c.cm. was injected into the pleura and the wound was closed, without drainage.

To exclude any possibility of injury to the stomach or intestine, the abdomen was opened by a high left paramedian incision. No damage was detected to the abdominal viscera and the parietal wound was closed in layers—with some difficulty due to the extreme obesity of the abdominal wall.

Post-operative abdominal distension and pneumonitis of the left lower lobe were responsible for a rather stormy convalescence for the first few days after operation, but they responded to routine general treatment. Sulphapyridine (M & B. 693) 4 grammes a day was administered for the first four post-operative days. Sedatives were given freely to allay cough and pain in the chest, and sleep was ensured by the administration of hypnotics. He was improving very rapidly till the 2nd May (7th post-operative) when a few loose motions were passed. Diet was restricted to fluids, and examination of the faeces revealed vegetative and cystic forms of *Entamoeba histolytica*. The next day the number of motions increased to 20 but administration of emetine and entero-vioform soon controlled his dysentery.

He was discharged perfectly well on 16th May, 1943, 20 days after admission.

The interesting point about the case is the prolapse of the omentum through the chest wall. A negative intrapleural pressure could easily explain the 'suction' of the omentum into the pleural cavity. The same mechanism can also explain its prolapse outside the wound. Inspiratory movements increased the intrapleural negative pressure and before the atmospheric air entered the pleural cavity, the diaphragm and the chest wall were brought nearer each other and the omentum, finding a track ready for it, occupied it. This is well in accord with the



habit of the omentum to find its way to the site of any mischief. A laparotomy was considered necessary as it was otherwise impossible to exclude injury to abdominal viscera.

## POST-MATURE PREGNANCY : A CASE REPORT

By J. K. MOHANTY

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H. D., aged 36, Hindu female, eighth para, was admitted into the Angul Subdivisional Hospital on the 14th May, 1942, with a history of difficult labour with prolapse of a hand. The duration of labour was 52 hours; prolapse of the hand occurred 8 hours before.

*Findings on admission.*—Patient well built and tall; in an exhausted condition; temperature 104.6°F., respiration 29 per minute; pulse 120 per minute; uterus asymmetrical, wider from side to side; no uterine contraction; delay apparently due to secondary inertia; foetus impacted and dead; oblique lie, dorso-posterior position with the head in left iliac fossa and breach on the right side; hand presenting, left hand lying in the vagina; bladder distended.

*History of present pregnancy and labour.*—The date of first day of last menstrual period was 4th July, 1941. The patient and her husband were emphatic about this.

There was nothing abnormal during the course of the present pregnancy except its length. Towards the end she felt unusual heaviness, discomfort and breathlessness. As the labour did not start after eleven lunar months, she and her relatives became alarmed. They sought the help of village quacks for the induction of labour, and with their medicines she had a number of watery motions on the 11th and 12th May, 1942, and labour pains started on the 12th afternoon. As labour was protracted, a country accoucher tried manual removal of the child on 14th May, but failed. The patient was brought to the hospital the same day.

*Previous pregnancies.*—All normal. All but the second child are living. The second child died of some unknown fever at the age of two. There was no history of abnormal duration of any pregnancy. Before this pregnancy the patient was regular in her menstruation, having a 26 to 30-day cycle. She had no pendulous abdomen and no uterine complaint.

*Management and treatment.*—The bladder was relieved by catheterization. The urine on examination was found normal. Before operation she was given glucose 25 per cent 25 c.cm. intravenously, subcutaneous saline one pint, sulphapyridine soluble 2 gm. intramuscularly, and morphine sulph. gr.  $\frac{1}{4}$  with atropine sulph. gr. 1/100 hypodermically. Under perhalation ether anaesthesia, decapitation was performed; the body and head were delivered, the latter by forceps with a little difficulty.

*After treatment.*—Pituitrin 10 units hypodermically was given immediately after operation; ergot powder gr. v thrice daily for three days, sulphapyridine in adequate doses for four days; intravenous glucose 25 per cent 25 c.cm.

twice a day for two days. Glucose sodium bicarbonate drink—*ad lib.* for two days. The temperature touched normal on the morning of the second day after operation, and remained so throughout. The subsequent history was uneventful; the patient was discharged cured on 22nd May, 1942.

*Child and its development.*—A male child; died a few hours before operation; blood not coagulated. Its weight was 9 pounds 6 ounces excluding the blood that was lost during decapitation; length 22 inches measured by approximating the decapitated head to the neck at the line of incision.

*Diameter of the child's skull.*—Sub-occipito-bregmatic—4 $\frac{1}{2}$  inches, occipito-frontal 4 $\frac{1}{2}$  inches; bi-parietal 4 inches and bi-temporal 3 $\frac{3}{4}$  inches.

*Circumference.*—Sub-occipito-bregmatic 12 $\frac{1}{2}$  inches and occipito-frontal 15 inches.

*State of ossification of bones.*—Centres of ossification of the upper epiphysis of tibia and humerus had already appeared in addition to that in the lower epiphysis of the femur. The cranial bones were unduly hard, and ossified to an unusual degree.

*Other signs.*—Hair more than one inch long; nails projected beyond the finger tips; both testes were in the scrotum.

*Discussion.*—The duration of pregnancy in the case reported in this paper is 315 days, reckoned from the first day of the last menstrual period. If calculation is made from the probable day of ovulation or fertilization, we may deduct from the period 14 or 15 days. Even then it comes to nearly 300 days, 30 to 35 days longer than the usual period of gestation. I believe the date of last menstrual period given by the patient is correct. The child definitely showed signs of post-maturity. Its length was 22 inches, which is longer by 2 inches than the average normal for Europeans.

Stone (1934) and Greenhill (1934) have given arbitrary figures of 9 pounds 10 ounces and 8 pounds 13 ounces as the minimum weight of a new born child to consider it as post-mature. These are European and American figures and will not hold good for Indians, whose average weight at birth is nearly 10 per cent less than that of Europeans. Moreover the figures are arbitrary. The average normal weight of a full term new born Indian baby is 5 $\frac{1}{2}$  to 6 $\frac{1}{2}$  pounds. The excessive weight in the case under report was surely abnormal; such a weight has not been recorded for a full term normal Indian child.

In a full term new-born, the lower epiphysis of the femur is the only epiphysis where beginning of ossification is present. In this case in addition to this, ossification had already commenced in the upper epiphysis of tibia and humerus. This is unusual and points to post-maturity. Of course very occasionally it has been recorded in full term babies, but whether those babies were full term or post-mature is questionable. The undue hardness and degree of ossification of the cranial bones is another point in favour of post-maturity.

The weight, the length, the state of ossification of different bones observed, together with other relevant points and the history put the question of post-maturity in this case beyond doubt.

Then the interesting but still unexplored question arises, why the labour did not come at full term? True post-maturity though not common is not unknown. It has been recorded in several cases by various authors. Its cause is most probably closely connected with the factors concerned in the initiation of labour. However, conclusive work on this point is still to be done. Many theories have been put forth as to the cause of onset of labour. Modern research workers are



exploring the endocrine system to find out its cause, and though their labour has not yet been crowned with success, the findings so far made suggest strongly that the true explanation lies there only.

Cohen *et al.* (1935) state that during the greater part of pregnancy 99 per cent of the oestrogenic material in the urine is in the combined ether-soluble form which possesses low physiological potency. Labour is accompanied by, and may be produced by, a fall in the combined form and a rise in the free form. Other workers hold the view that a factor in the initiation of labour is the interference with the normal mechanism of inactivation. It has been observed that injections of free active oestrin into the pregnant animals lead to abortion. The same result has been obtained in human beings. Charlewood (1938) advocates injection of oestrin for the induction of labour.

Some authorities are of the opinion that patients in whom pregnancy continues beyond term possess a refractory neuro-muscular mechanism, as in them induction of labour often fails. But what makes their neuro-muscular mechanism refractory? One hesitates to accept the idea that they inherit a defective neuro-muscular system, in view of the observed fact that, in any individual, not all but only one pregnancy is at times prolonged beyond the usual term. This is the fact in my case. If some disturbance in the endocrine system is the cause of post-maturity, what causes this disturbance?

It is also known that progesterin in combination with oestrin desensitizes the uterus to the action of oxytocin. As pregnancy advances, the influence of progesterin wanes and the uterus becomes sensitive to the action of posterior pituitary hormone, as the result of which its spontaneous contractility increases and may culminate, with the concomitant involution of the corpus luteum, in onset of labour pains.

Biological findings have demonstrated that, just before the start of labour, there is a fall in the oestrin content of blood. Clinically it has been observed that sudden withdrawal of oestrin after its administration for some days results in uterine bleeding. Thus the inference has been made that, physiologically, withdrawal of oestrin just before labour might be the cause of onset of labour.

Whatever may be the endocrine mechanism in the initiation of labour, some interference in its physiological process most probably contributes to the prolongation of pregnancy beyond term; but this matter remains still indeterminate and controversial.

Post-maturity is fraught with dangerous consequences. It becomes a grave and definite risk to the lives of both mother and child. Invariably it causes difficult labour and very often abnormal presentation. In the present case, with the oblique lie, the hand presentation, impaction of the foetus, and the patient staying in a remote village where immediate medical aid was not available, death would surely have occurred had not secondary inertia of the uterus supervened.

*Acknowledgment.*—My gratitude is due to the Superintendent, District Jail, Angul, for sanction for the publication of this article. I am also grateful to Dr. G. C. Pattanayak, Civil Assistant Surgeon, Angul, in whose absence I performed the operation and who helped me with valuable suggestions in the preparation of this article.

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## A CASE OF NEUROMYELITIS OPTICA (DEVICS' DISEASE)

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NEUROMYELITIS optica is a variety of acute disseminated encephalomyelitis. It affects all ages; according to some authors more commonly young females. Pathologically the disease resembles disseminated sclerosis in that there is demyelination of axis cylinders. The spinal cord shows such diffuse or multiple disseminated lesions. The optic nerves also present the same type of lesions. Clinically the disease is quite distinct from disseminated sclerosis. It is characterized by an acute onset of paraplegia and optic neuritis. Either the paraplegia may develop first or the blindness. The prognosis is said to be favourable in about 50 per cent of the cases. If the progress of the paralysis stops, there is great likelihood of complete or partial recovery of the paralysis and also of the vision. In other cases the paralysis gradually extends and involves respiratory muscles. The cause of the disease is not known; it is believed to be some virus or metabolic toxin. There is no known treatment for the disease. The disease is said to be a rare one.

The following case was recently admitted into the wards of the Rajendra Hospital.

*History.*—A Muslim female, aged 35 years, was admitted on 7th September, 1943. She complained of complete blindness of both eyes. About four days before admission she suddenly developed vomiting at night. Next morning there was hiccup which lasted throughout the day and in the evening she noticed some dimness of vision. In a few hours this developed into complete blindness. While in the hospital, about six days after the beginning of her illness, she developed weakness first of the right leg and then of the left; there gradually developed a complete paralysis. The paralysis gradually extended upwards. After two or three days her upper extremities were also involved and she felt great difficulty in respiration. She developed retention of urine and faeces. Her relatives took her home on 12th September, 1943, where she died the next day; a post-mortem could not be done.

*Examination.*—On examination while she was in the hospital she showed complete blindness. Examination of the fundus revealed slight congestion of the disc but no papilloedema. Both the pupils were completely dilated and did not react to light or to accommodation. The movements of the eyes were normal. There was slight paresis of the lower half of the face on the left side. Other cranial nerves were intact. The upper extremities were partially paralysed with increased jerks. The abdominal reflexes were absent. The lower extremities showed the upper-motor-neurone type of paralysis with increased jerks and an extensor plantar reflex. There was complete loss of sensation below the level of the third intercostal space. The Wassermann reaction of blood and cerebro-spinal fluid were negative. Cerebro-spinal fluid showed normal cytology.

## Acknowledgment

My thanks are due to Dr. Abul Hassan, my house physician, for careful record of the case.

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## Indian Medical Gazette

JANUARY

## VITAMIN C\*

VITAMIN C is a most interesting member of the ever increasing family of vitamins. Scurvy which is caused by the lack of it has been recognized for centuries, but modern work dates from 1907. The vitamin was isolated in 1928 and the story of its isolation is an amusing one.

In 1928 Szent-Györgyi actually isolated vitamin C from cabbage and adrenals without knowing it during the course of studies on cellular oxidation. He called it 'ignosic' acid because it resembled a sugar that he called 'ignose'. When the editor of the journal to whom his report was sent objected to 'ignose', Szent-Györgyi altered it to 'Godnose'. This was equally objectionable to the editor and the name was finally altered to 'hexuronic acid', which was later identified with vitamin C. 'I became a father', said Szent-Györgyi, 'without wishing it, the father of a vitamin. Such accidents seem to happen in science.'

The formula was established in 1933 and later in the same year the vitamin was synthesized.

Vitamin C is remarkable for the large number of ways in which its presence or absence in reasonable amounts is said to influence the functions of the body in normal and abnormal circumstances. It appears to be well established that it has an important rôle in the formation of intercellular substance—the reticulum and the collagen. This action is not confined to the soft tissues but is also seen in dentine, cartilage, bone and also the capillary walls. There is however little clinical evidence that dental decay is due to vitamin-C deficiency, although bleeding, soreness of the gums and loosening of the teeth are seen in vitamin-C deficiency. The influence of vitamin on bone formation is seen by the fact that the union of fractures is very much delayed if not completely absent in vitamin-C deficiency.

Many reports have been made regarding the action of vitamin C in encouraging wound repair. Crandon† carried out on himself a most remarkable experiment. He placed himself on a vitamin-C free diet supplemented by all the other known vitamins. He continued the experiment for no less than six months and developed well-marked scurvy. During these six months he carried out on himself numerous experiments and made many observations, some of which are mentioned here. One experiment was on the healing of wounds, and the results were very clear cut, indicating that vitamin C was essential for rapid and sound healing. In its absence, as a result

of the inadequate collagen material; the whole architecture of the wound was disturbed.

The hæmorrhagic manifestations of vitamin-C deficiency have been attributed to abnormal capillary fragility possibly caused by the absence of intercellular material. Crandon's experiments however gave little support to this idea. Even after five months on scorbutic diet, when the petechiæ has begun to appear over the leg, the application of a blood-pressure cuff blown up to 100 mm. of mercury brought out no more petechiæ than in normal controls. Recent work has suggested that vitamin P plays a part in the control of capillary fragility; vitamins C and P are often found together in foodstuffs.

It has been considered that vitamin C influences the formation of hæmoglobin and the maturation of red cells, and anæmia is often associated with scurvy. In humans, however, evidence on this matter is conflicting. Crandon after six months on scorbutic diet developed no definite anæmia. A tendency to fall in hæmoglobin in the third month was controlled by the administration of ferrous sulphate. Other workers have however reported the occurrence of anæmias which respond to vitamin C without any other treatment, or even after failure to respond to iron.

Another important action of vitamin C is said to be in infective processes. There is no doubt that infection greatly increases the body requirements of vitamin C, and this fact indicates the need for giving increased amounts of this vitamin to persons suffering from infections. Moreover, there is evidence that vitamin C is important in encouraging the production of antibodies. There are numerous reports on this matter, which cannot be discussed here. The administration of vitamin C to experimental animals is said to increase the production of agglutinin, hæmolysin, precipitin and complement. This matter is important to laboratory workers.

Some workers have considered that vitamin C is of very considerable importance in the prevention of infection, and various studies have been made on the incidence of common cold and tonsillitis in large groups of people, some with an adequate intake of vitamin C and some without. Early reports indicated a significant difference suggesting a protective action of vitamin C, but recent carefully controlled work has not borne out this idea.†

It has been reported that vitamin C has a definite action in encouraging leucocytosis. This idea was substantiated by Crandon's observations. During his period of scorbutic diet his white cell count fell from 5,000 to 3,500, and after one injection of 1,000 mg. it rose to

\* Much of the information given here is quoted from the book on 'The Vitamins in Medicine' by Franklin Bicknell and Frederick Prescott, published by William Heinemann (Medical Books) Limited, London, in 1942.

† Crandon, J. H., Lund, C. C., and Dill, D. B. (1940). 'Experimental Human Scurvy.' *New Eng. J. Med.*, **223**, 353.

Crandon, J. H., and Lund, C. C. (1940). 'Vitamin-C Deficiency in an otherwise Normal Adult.' *New Eng. J. Med.*, **222**, 748.

Cowan et al. (1942). *J. Amer. Med. Assoc.*, **120**, 1268.

5,000 and later to 9,000. Other work in human beings has indicated a similar action, and the low resistance of people suffering from scurvy has been attributed in part to the lack of leucocytes.

During recent years, workers in various countries have reported another important action of vitamin C, namely, as a detoxicating agent particularly towards the neo-arsphenamines. Evidence in human subjects on this matter is very conflicting. From 1939 onwards this matter has been studied and reported upon by various workers, and in India, recently, similar reports have been made by at least one worker. Some workers have reported a similar detoxicating action of vitamin C during the administration of lead, gold, sulphonamides and other drugs.

From 1936 various reports were made on the relation between vitamin C and the activity of the ductless glands. There is said to be a relationship between the activity of the adrenal cortex and the vitamin-C content, and the administration of vitamin C is said to increase adrenaline production. Vitamin C has also been reported to oppose the action of the thyroid gland. A connection between vitamin C and progesterone has also been reported, and it has also been stated that the administration of vitamin C activates the gonadotropic hormones.

Many reports have been made on the influence of vitamin C on carbohydrate metabolism. Studies in animals indicated that when administered by the mouth vitamin C had no effect on the blood sugar level, but when given intravenously it caused a fall in the normal individual. Reports of studies in diabetics however have been conflicting.

Bicknell and Prescott refer to numerous papers bearing on this subject which have been published during the period since 1935, and in discussing results, they make the following comments :

'Much of the work done on vitamin C and carbohydrate metabolism has been uncritical. Either observations have been made on the immediate effects on the blood sugar level of a single intravenous or oral dose of the vitamin, or the effect of vitamin C on diabetics who have recently come under control has been observed. The fallacies are quite obvious. The injection of any foreign substance into the blood stream in relatively large quantities may temporarily affect the carbohydrate storage mechanism of the liver or alter the permeability of the kidney glomeruli to glucose. Vitamin C has also been given to uncontrolled diabetics at the same time that a diabetic regimen was instituted. The fact is disregarded that the tolerance of any diabetic improves under treatment, and any beneficial effects that resulted were attributed to the new form of therapy used. In some cases small laboratory animals were used to test the effects of vitamin C. These animals are notorious for the variety of manifestations which they show when placed on deficient or unnatural diets, and it is not surprising that their carbohydrate metabolism was upset. Possibly other biochemical estimations would show considerable abnormalities.'

Certain work bearing on this subject is now being done and published in India, and workers would do well to study this earlier work

thoroughly and to bear in mind the fallacies mentioned above.

These are only a few of the actions which have been attributed to vitamin C; many other actions have been suggested. Further work is needed to clear up many doubtful points. .

## INCOMPATIBILITY OF SULPHONAMIDES AND QUININE

THE following note appeared in a recent issue of the *Lancet*. As far as we know, no publication on this subject has as yet appeared in India. On several occasions recently we have been tempted to administer simultaneously quinine and sulphonamide, particularly in one case with both pneumonia and benign malaria. Having read this note, we decided to treat the pneumonia first and the malaria second, a procedure which proved quite satisfactory.

We feel that physicians in India should be aware of the possible danger of giving quinine and sulphonamide at the same time.

Recent work suggests that the sulphonamides should be avoided when quinine is being given. Niblock observed that in 6 patients treated with quinine and sulphonamides simultaneously vomiting occurred in every case and recovery was slower than was expected. Pharmacological confirmation of this clinical observation comes from Harned and Cole, who have shown that in rats . . . idine and quinine the absorption of . . . is increased on the average by 44 per cent, and there is a corresponding rise in the amount of acetyl-sulphapyridine in the urine. The largest dose of quinine given almost doubled the output of acetyl-sulphapyridine. They found no corresponding rise in the volume of urine secreted during these experiments, and this curious effect of quinine must therefore increase the risk of deposition of crystals in the kidney tubules. It would be interesting to know whether sulphonamide-quinine therapy in the human subject produces impairment of renal function, for Niblock's observations taken with those of Harned and Cole raise the possibility that this combination of drugs may produce uramic symptoms. When mepacrine hydrochloride ('atebrin') was substituted for quinine in the experiments on rats the alterations in absorption and excretion of sulphapyridine were not observed. In this country the occasions when sulphonamides and quinine are used together for combined malarial and bacterial infections must be rare. But in tropical and sub-tropical countries this incompatibility will have to be borne in mind.

## Special Articles

### SURVIVAL AFTER SHIPWRECK

By R. N. CHAUDHURI, M.B. (Cal.),  
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ONE HUNDRED AND FIFTY YEARS ago a seaman's guide was published which collected together various accounts of survivors from shipwreck.

Much of the advice given in it still holds good to-day, but it is surprising that the medical aspects of the subject have been little studied until the present war. Two years ago the Medical Research Council appointed a committee to enquire into the physiological problems that arise out of exposure to the sea after loss of ships or aircraft and frame practical recommendations. The result of the inquiry is War Memorandum No. 8 (*A Guide to the Preservation of Life at Sea after Shipwreck*, His Majesty's Stationery Office, pp. 11, 4d.) which combines practical experience with the results of research and which is so interesting that we give a detailed summary below.

The comfort and indeed the chances of survival of those adrift depend on the frame of mind of the boat's company and this again depends on the bearing and conduct of the officer in charge. Strict discipline must be maintained and bodily energy should not be wasted by useless exertion. Recent statistics show that of boats adrift for more than 24 hours, nearly half have reached safety within 5 days and it is exceptional for any life-boat not to be picked up within 3 weeks.

The memorandum sets out the routine preparations in the ship, which include regular inspection of the various life-saving appliances with special attention to water and food containers, first-aid outfits, etc. In abandoning a ship, every effort should be made to carry extra water, as water is more important than food. Oil drums half-filled with water can be stored on the deck ready to float off or be rolled overboard. Each man should fill and take with him a water bottle. Extra clothing, both warm and waterproof, is very necessary and should be gathered up, as it protects not only against the cold but also against the sun. Even in the tropics it may be bitterly cold at night. Men are reminded that they are unlikely to need more food than is stored in the life-boat, and no extra food should be taken at the expense of extra water and extra clothing.

### *Thirst and hunger*

Once on board the rescue-raft, the chances of winning through have improved enormously. Every one in the boat excepting the badly wounded or the very exhausted will be given a job to do. Survival will depend on every one carrying out his routine cheerfully and promptly. Instructions are given in the memorandum regarding care of feet and protection against cold, rain, sun and heat. One can bathe once or twice a day but should take care to avoid being bitten or stung by marine creatures.

The officer in charge should take stock of his water supply, should plan its rationing according to the stock; number of men, time likely to be adrift and chances of catching rain water, and control its issue from the start. The present water supply in life-boats gives each man of

the boat's full complement  $5\frac{1}{2}$  pints. If the company is likely to be picked up more or less immediately, a generous supply can be issued at once; if delay in being found is likely, there is no need to give any water at all during the first 24 hours unless the men have been sweating from hot weather or heavy exertion, when the issue of water should begin at once. The Medical Research Council recommends 18 oz. per man daily until there is one pint per man in hand, then the ration should be reduced to 2 oz. per day. This system of rationing is based on the fact that man's minimum requirements of water are at least 30 oz. per day. It has been found by experiment that 18 oz. of water per day is the smallest amount needed to keep a man fit for periods customary in life-boat trips. The usual ration of 2 to 8 oz. per man daily falls so short of the body's needs that rapid and progressive deterioration sets in if it is enforced. Besides it is foolish to ration water on, say, a 60-day basis when the chances of being picked up in 10 days are good. Quite often men are picked up in poor condition owing to low water rations, with considerable stocks of water still in the boat. Experience suggests that it may be helpful to moisten the lips and rinse out the mouth with sea water but it must not be drunk, being definitely harmful to life. If rain falls, the water can be collected in canvas gear or any vessel that is available. The drinking of urine is harmful and should be prohibited.

When water rations are low, the food ration should consist mainly of fats, starches and sugars, and contain only small amounts of protein and salt. Fats are the most concentrated energy-bearing foods, and allay hunger better than any other types of foodstuffs. Hence a biscuit with a high fat content is recommended. The best kind of fat is pure butter fat; chocolate and condensed milk are favourite and desirable articles of diet. Meat and other foodstuffs rich in protein increase the body's requirements of water, and should be avoided. A suitable diet for each person per day includes 1 oz. each of high fat-content biscuits, condensed milk, chocolate and butter fat. It will not stop loss of weight but it will prevent hunger.

Certain habits must be cultivated if best use is to be made of the limited resources. Water and food should be issued at regular hours, say three times a day. Men are advised to make the most of each share-out of water by keeping it in the mouth for a long time so as to rinse the mouth, gargling and then swallowing. Biscuits may be broken up and the pieces kept in the pockets; they can be nibbled throughout the day. Condensed milk is best taken by itself one hour before the water ration. Spirits, e.g. whisky, brandy or rum, if available, are to be kept for the wounded. Smoking may increase thirst but heavy smokers may find it soothing. It is important to get regular sleep during watches off. With increasing fatigue, however, it is difficult to keep awake.



### *Energy tablets*

These tablets contain 5 mg. of either methedrine or amphetamine. Their action is to lessen feelings of fatigue and exhaustion, promote alertness, raise the spirits and prolong the will to live. They should be regarded as a stand-by when hardship is beginning to wear men down and this cannot be remedied by encouragement, rest or sleep. They may be given at the rate of 2 tablets three times a day or less often according to the men's condition. Single doses of 2 tablets may be given at any time when a special effort is necessary, i.e. a spell of hard pulling to make for land. The tablets should not be given to wounded men, to excitable or hysterical men or to those whose minds are wandering.

### *Frost bite and immersion foot*

Of the ailments which may occur from exposure, these two may here be mentioned. In frost bite the skin and sometimes deeper tissues become actually frozen. At sea it is very rare unless the sea water is freezing. Wind encourages it. The damage is caused by minute crystals of ice which form within the skin; the fingers, ears and nose are the parts most likely to freeze. The skin becomes pale and yellowish white, looks unusually opaque and feels of wooden hardness; this hardness is the only reliable sign of freezing. Prevention consists in keeping as warm as possible with plenty of clothing, thick gloves and ear protectors. The feet and socks should be kept dry and the feet kept moving to maintain the circulation. Greasing the exposed parts with oil or vaseline is useful. The company should watch each others' faces for the first signs of frost bite. Small frozen areas may be thawed rapidly by covering with a warm hand. Frost-bitten skin must not be rubbed with snow.

Immersion foot, which is not the same thing as frost bite, is due to immersion of the feet or legs for many hours in cold water or mud. Sea water cold enough to injure is usual in the Atlantic (winter and summer) from latitude 50° northwards. The part is distinctly painful and later becomes red, numb and swollen. These signs quickly disappear if immersion ends and the limb can be warmed; otherwise the damage will become more serious by the formation of blisters, dark patches and broken skin. For prevention, men are advised to keep the feet out of water by keeping the bottom of the boat as dry as possible, or by raising the feet. The feet and toes should be frequently moved. Any rubbing should be done very gently and the part should not be exposed unless it is fairly warm. Greasing the feet is not of much use. It is very important to keep the upper parts of the body warm and it is better to keep on damp clothes under waterproof covering than to strip and wring out the clothes in a cold wind.

### *After rescue*

After being picked up, the crew would first of all require drink, food, warmth and sleep. It is better to be sparing in the consumption of food at first; something light and easily digestible should be chosen. The legs will require attention. In cases of frost bite, the best way of thawing the part is to put it in cold (not warm) water with the rest of the patient warmly wrapped up. Rubbing with snow or otherwise is dangerous. If pain is severe on thawing, cool the part again for a while with cold water, ice or snow. After thawing, warming must be very gradual; it is dangerous to apply hot-water bottles or warm the limb in front of a fire. It should be gently cleaned and dried, dusted with sulphanilamide, wrapped in clean material and kept at absolute rest. Treatment of immersion foot must begin immediately after rescue. The patient should be wrapped up in warm blankets and hot bottles placed near the body but not near the affected limbs which should always be kept cool by the use of fans or even ice if necessary, but the ice should not be brought into direct contact with the skin. The temperature of the skin should be reduced to 80°F., but not below 70°F.; it can be measured by placing a bath thermometer against the skin. The limb will swell again if allowed to warm too soon. Warming up must be gradual and heating or rubbing is harmful. Treatment must be continued until all swelling has gone and the patient is able to walk without pain. The feet and legs are to be kept dry and nothing should be applied except sulphanilamide powder and a clean dry cloth cover.

Surgeon Captain Macdonald Critchley's book on the same subject (*Shipwreck Survivors, A Medical Study*, by Macdonald Critchley, M.D., F.R.C.P., J. & A. Churchill, Ltd., London, pp. 119, 7s. 6d.) constitutes the Bradshaw lecture, 1942, delivered to the Royal College of Physicians, London. It describes, in addition to the various ordeals suffered by men, the clinical effect of these privations and the physiological problems involved and should be read in conjunction with the M.R.C. pamphlet. These are discussed under the following heads: (1) excessive cold and wet, (2) thirst, (3) hunger, (4) tropical conditions, and (5) psychological effects. We give a brief description of some of the points.

Cold is the most distressing and dangerous hardship, and its effect is often aggravated by high wind, wetness, etc. It tends to overwhelm a man in a comparatively short time, the train of clinical events seeming to be shivering, headache, increasing reluctance to move, an attitude of generalized flexion, drowsiness, torpor and death. How long one can survive in excessively cold conditions is not yet known for certain; sailors and marines are as a class relatively insensitive to cold up to a certain point, and large persons withstand cold immersion better than small. Children prove highly susceptible to the effects of extreme cold.

An inadequate supply of drinking water constitutes, after cold, the greatest hardship. The longest time that has been endured without water after shipwreck is probably eleven days. The overwhelming thirst may compel the victim to drink fluids which he would ordinarily abhor, blood, sweat, urine, etc., but the most important complication is the drinking of sea water. This acts as a poison to a dehydrated person and is, after cold, the commonest cause of death in shipwrecked persons. It increases thirst, later delirium sets in, often of violent type, consciousness is gradually lost and death takes place quietly. The condition is probably due to a rapid and severe increase in the degree of dehydration owing to inability of the kidneys to cope with large amounts of salt. Food is of secondary importance in shipwreck conditions. Adequate water is the dietetic factor which determines survival. The testimonies of shipwrecked seamen show that while thirst is complained of, hunger generally ceases to be clamorous after the first 36 to 72 hours.

In a recent publication, attention has been drawn to the great value of fish juice as a source of fluid for survivors after shipwreck, and it is stated that life-boats are being provided with fishing tackle to enable them to catch fish. The fish caught is cut into pieces and the body fluid of the fish is then squeezed out either mechanically or else by chewing with the teeth. The body fluid is said to be perfectly fit for human consumption, to contain a relatively small amount of salt, to be appreciable in amount and to be of considerable value in the relief of thirst. This however is not mentioned in this book.

Exposure in tropical latitudes is much better tolerated. The main discomfort is thirst. Oedema and numbness of the feet and ankles, dermatitis, blisters, etc., may develop. Sharks, although a source of anxiety, are perhaps not so dangerous as usually imagined. When they rub against the life-boat, they are probably trying to rid themselves of sea-lice. More important than sharks are some other carnivorous fish such as barracuda (tiger fish) and blue fish, these are very ferocious and destructive. Contact with jelly fish (Portuguese men-of-war) may cause pain 'like falling into a bed of nettles' and one man who got entangled among its tentacles said 'it was like being electrocuted'.

Various psychological phenomena may occur and are described in an interesting chapter. At the time of rescue, the men may present a varying picture, depending on the degree of privation and their mentality. In the absence of complications such as immersion foot, speedy recovery is the rule. Seldom we see those traditional 'sequelæ of exposure to cold and wet' such as rheumatism, neuritis, fibrositis, etc.

The book is of absorbing interest and is enriched with many historical facts and examples from the present war and has some photographs to illustrate various lesions.

## A CLINICAL STUDY OF FIFTY CASES OF MENINGO-VASCULAR SYPHILIS

By B. K. RAMAKRISHNA RAO, B.Sc., M.B., B.S.,  
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*Introduction.*—The subject of neuro-syphilis is of great importance to the clinician, since it is the commonest organic disease of the nervous system. Brain (1940) (England) states in his book on 'Diseases of the Nervous System' that neuro-syphilis occurs in about 10 per cent of persons infected with *Spirochæta pallida*. Grinker (1936) (America) says that 'about 25 per cent of all syphilitics develop some form of neuro-syphilis'. These figures apply to all forms of neuro-syphilis. Collier and Adie (1937) (England) say that 'cerebrospinal syphilis (excluding tabes and general paralysis) occurs in about 4 per cent of all persons who acquire syphilis'. I have not been able to obtain statistics for India.

On purely clinical grounds a distinction has long been made between two groups of tertiary neuro-syphilis; one which has been called interstitial, meningo-vascular, or cerebrospinal syphilis, and the other, which includes tabes and general paralysis, is commonly known as parenchymatous syphilis, para-syphilis or meta-syphilis. In the former, namely, meningo-vascular syphilis, the symptoms usually appear within three to four years of infection; the lesions tend to be focal and usually respond fairly well to treatment; whereas in tabes and general paralysis, the incubation period is much more prolonged, there are diffuse or systematized pathological changes, and response to treatment is poor.

The names which have been applied to the two varieties of neuro-syphilis may be unsatisfactory, since we are ignorant of the correct basis of this clinical distinction. Neither the involvement of the meninges and blood vessels nor a cerebrospinal distribution is exclusively peculiar to the more benign form; nor is the destruction of the parenchyma of the nervous system limited to tabes and general paralysis. McIntosh and Fildes (1914-15) have cogently put forward the view that in meningo-vascular syphilis, the essential lesion is in the blood vessels and the meninges, and that the parenchyma is only involved secondarily; whereas in tabes and general paralysis, the nervous parenchyma is itself invaded and there is a mesoblastic reaction. This hypothesis justifies the use of the term meningo-vascular syphilis as a convenient term for the more benign form of neuro-syphilis, and of the term parenchymatous neuro-syphilis for tabes and general paralysis. The distinction between the two forms of neuro-syphilis is also justified from the variability of their incidence in different countries. In India, for example, while meningo-vascular

syphilis is very common, parenchymatous neuro-syphilis is rare indeed. I have seen only three cases of tabes dorsalis during the past six years. As for G.P.I., I remember of only one case that was demonstrated to me by my professor of medicine, when I was a student of the Medical College, Mysore, in 1932. I have not had the opportunity of seeing a single case of G.P.I. in my general practice. A few cases may be found in mental hospitals.

On the other hand, while the so-called para-syphilitic nervous manifestations are very rare in India, the para-syphilitic manifestations of cardio-aortic syphilis such as aneurysm, occurring ten to twenty years after infection, and rarely responding well to treatment, have been quite common in my experience.

The idea of the dual nature of the spirochæte itself, that there are neurotropic and dermatropic strains, as claimed by Levaditi, and the suggestion of Orr and Rows that the path of infection, hæmatogenous or lymphogenous, may have an influence on the type, character and course of neuro-syphilis, I do not feel competent to discuss. In brief it may be stated that there is a constellation of factors operating on the incidence and course of neuro-syphilis. The biologic properties of the spirochæte, the constitution of the infected individual, his environmental, and the various toxic and traumatic factors to which he may be subjected to, may all influence the clinical manifestations of neuro-syphilis. All these factors are vague and indeterminate. That there are still many unsolved problems in neuro-syphilis is beyond dispute; and it is aptly remarked that 'to know the problems of neuro-syphilis is to have an adequate grasp of clinical neurology'.

*Ætiology.*—Though syphilis has been prevalent with us for centuries, and headache and palsies were attributed to it even in the Middle Ages, it is only during the present century that we have gained much knowledge about the causal organism and its protean manifestations. This we owe to certain epoch-making discoveries during this century. The discovery of *Spirochæta pallida* by Schaudinn and Hoffmann in 1903-5, and the experimental transmission of the disease to apes by Metchnikoff in 1904, proved Koch's postulates. The elaboration of the Bordet-Wassermann reaction during 1901-7 made the diagnosis much simpler. Neuro-syphilis, however, was for a long time considered to be an affection beyond the category of systemic syphilis. There were theories that the nervous lesions were toxic or allergic, and that the spirochæte itself did not invade the nervous tissues. The now obsolete terms such as meta-syphilis and para-syphilis are evidence of the then current theories. It was only in 1913, when Noguchi and Moore and McIntosh and Fildes (1914-15) demonstrated spirochætes in the brain, that the direct and specific infective basis of neuro-syphilis was recognized.

It is often very difficult to obtain a positive history of a primary lesion from a patient suffering from neuro-syphilis. The nervous manifestations may occur long after the initial infection and he may have forgotten all about it; or, after such a long period of well-being, the patient is unable to attribute his present malady to a previous indiscretion. Again, some patients may repress the information voluntarily and expect the physician to assume that his malady may be due to a specific infection. It is also possible that the patient might have considered the ulcer as traumatic when it was really syphilitic. Further, it is well known that there are genuine cases in which the primary lesions have been inconspicuous or entirely absent. As for the symptoms of the secondary stage, such as sore throat, dermal eruptions and arthralgia, such a history can rarely be elicited from patients suffering from neuro-syphilis. Such a negative history is more common in parenchymatous syphilis than in meningo-vascular syphilis.

In my fifty cases I was able to obtain a history of primary sore in seventeen cases. As for a history of the symptoms of secondary syphilis, I was able to elicit it in only three cases.

*The latent interval.*—All the cases in which I was able to get a history of primary sore came under my observation within three years of infection. The average interval in ascertainable cases has been about 15 to 18 months. Cases in which vascular cataclysms occur seem to have a much shorter latent interval. Out of the eighteen cases of cerebral thrombosis, eight came within one year of infection. The acute forms of myelitis also seem to have a very short latent interval. Out of six cases of transverse myelitis, three came within one year of infection.

*Age incidence.*—The oldest patient of my series has been 45 years old, and the youngest 20 years. The majority of my cases were between 25 to 35 years of age.

*Sex incidence.*—Out of my fifty cases, only nine were females, but the number of female medical beds in the Sri Krishnarajendra Hospital, Mysore, where I have been working, is only half the number of male medical beds. Moreover, many female patients go to the female out-patient department, since some of them prefer to be treated by a lady doctor. Therefore it is probable that the real incidence of the disease is higher in the females than my figures suggest. Moreover, the female cases that I have seen in the hospital are the more severe cases, such as hemiplegia and paraplegia, needing hospitalization either on account of the acuteness of onset or inability to walk. The milder and less acute types are unlikely to be admitted to the hospital as in-patients.

*Pathology.*—The purpose of this paper being mainly a clinical study, I will mention only briefly the essential lesions. Every syphilitic

lesion commences with the collection of spirochaetes around the small arteries. This is followed by an inflammatory reaction with oedema and exudation of lymphocytes and plasma cells around the small vessels. This initial periarteritis is followed by invasion of all the coats of the artery, giving rise to a pan-arteritis and usually proliferative endarteritis which may cause one of the most dangerous consequences of the disease, namely, thrombosis. Later on, the walls of the vessel may become fibrosed. This characteristic reaction of the mesoblastic tissues to the spirochaetes is the pathological basis of meningo-vascular syphilis. Spirochaetes are very scanty in the lesions, and it is only with great difficulty that they can be demonstrated.

*Classification.*—Interstitial syphilis is usually classified as cerebral and spinal depending upon the main anatomical localization. It is again subdivided into meningeal, and vascular, for purposes of convenience, though the majority of cases are really meningo-vascular. Of my fifty cases, thirty-four have been cerebral and sixteen spinal. Two cases were really cerebrospinal.

#### *Cerebral syphilis (thirty-four cases)*

*Clinical features.*—The symptoms of cerebral syphilis are by no means pathognomonic, since identical pictures may be produced by other lesions. For example, hemiplegia resulting from syphilitic endarteritis may not differ essentially from hemiplegia caused by thrombosis of an atheromatous vessel. Fits and cranial nerve palsies can be produced by tuberculous infection or neoplasm. But the study of the particular combination of symptoms is very useful, for syphilis has its own peculiarities. The main lesions of the disease may be vascular or meningeal; the lesions may be diffuse or localized in any portion of the brain, or cranial nerves may be involved either singly or in any combination; therefore, a combination of symptoms is usual. In many cases it is the multiplicity of symptoms, their presence in unusual combinations, and the changes in their intensity and distribution from time to time that give the clue to a correct diagnosis.

*Prodromal symptoms.*—Often some of the symptoms act as forerunners of the more serious ones to follow. Of these the commonest are headache, insomnia, fatigue, and mild changes in the temperament. Headache is the commonest. It has been present in more than half of my cerebral cases. The headache is often worse at night, and is subject to periodic exacerbations. It may be unilateral or bilateral, frontal or occipital, or it may be shifting in character. Such cephalalgias may precede a vascular accident for days or weeks. In very rare cases headache has been the sole symptom of neurosyphilis. Insomnia and restlessness are also common. Changes in the temperament, such as irritability, depression, unusual exaltation, lack of concentration and confusion, are not

uncommon. Four of my cases came under my observation during this prodromal stage. All of them progressed quite well since they were detected early—the Wassermann reaction being positive. In my experience these prodromal symptoms seem to be more common in meningeal types than in patients who come to the hospital on account of vascular accidents.

At any time, with or without the premonitory symptoms mentioned above, other definite symptoms of intracranial mischief may become manifest. Of these the commonest are cranial nerve palsies, fits and vascular thrombosis.

*Cranial nerve palsies.*—The commonest nerve to be affected is the 3rd nerve, and next to it the 6th. These cases are more likely to be seen by the ophthalmic surgeon. Next in order is the affection of the 7th nerve. The 5th is also involved sometimes. The other cerebral nerves also may be involved, and it is not uncommon to get them affected in combination.

Of my thirty-four cases of cerebral syphilis, six came under my observation for cranial nerve palsies. Two had facial palsy, one had affection of the 7th and 8th nerves, one had involvement of the 5th, and two involvement of the 6th. It is sometimes very difficult to distinguish a 7th nerve paralysis due to syphilis from Bell's palsy. In fact, both of my cases in which the facial nerve was involved were referred to me as cases of Bell's palsy. A distinction between them may be extremely difficult unless serological reactions come to our aid. But a syphilitic subject is not immune to Bell's palsy. In this connection, I would like to point out that in syphilitic cases there is often a prodromal period of headache. Moreover, the onset of facial paralysis in syphilitic cases is more insidious than in Bell's palsy. A paralysis which takes more than 24 to 48 hours to develop is not Bell's palsy. In both of my cases this point gave me the clue for further investigation. The onset of the paralysis in both my cases was very gradual, it took several days for its development, and in the earlier phases it was intermittent. Of course, in syphilitic cases there may be other associated lesions. Both these cases improved quite well with anti-syphilitic treatment.

The involvement of the 5th nerve was found in a young man of 25 years of age who was referred to me as a case of trigeminal neuralgia. He complained of severe attacks of pain over the whole of the left side of the face. A simultaneous affection of all the three branches of the 5th nerve is practically unknown in trigeminal neuralgia. Further, clinical examination showed that there was paresis of the left 6th nerve and there was involvement of the motor division of the 5th nerve as revealed by loss of power in the left masseter and temporalis, which of course cannot occur in trigeminal neuralgia. I could not detect any facial weakness. Lumbar puncture was done. The patient had a severe exacerbation of pain after a few hours and he developed facial paralysis. Attributing the

worsening of the condition to the lumbar puncture, the patient went away, protesting that he was unsafe in my hands. I do not know how he has fared. The C.S.F. showed pleocytosis and the W.R. was highly positive.

*Fits.*—At any time, with or without prodromal symptoms, the patients may exhibit more dramatic symptoms such as fits. They may be general or focal. Three of my cases came for generalized convulsions, and clinically a tentative diagnosis of meningitis was made on account of the associated cervical rigidity. Two of the cases showed signs of optic neuritis on ophthalmoscopic examination; one had congestion. It is worth while to remember that idiopathic epilepsy rarely commences after the teens. If a young adult comes with convulsions, an organic cause such as syphilis or tumour must be thought of. A correct diagnosis can be arrived at only by further detailed examination, particularly of the cerebrospinal fluid. All the three cases that came for general convulsions had a raised pressure in the C.S.F. There was extreme pleocytosis, both of lymphocytes and polymorphs, and the Wassermann reaction was positive. Two of them died and one recovered. Only one case came for local fits. A young football player, aged 20 years, found that after a strenuous game of football his right foot was 'funny' (pins and needles) and that he could not use it properly. He went home and got it massaged. He felt better the next morning. But towards the evening he found that he could not play football, since his right foot began to stick to the ground. He went home and found that the right foot began to twitch involuntarily. When he came to consult me the next day there was slight weakness of dorsiflexion of the right foot and the plantar reflex on the right side was doubtfully extensor. During the course of the examination the right foot began to twitch and this twitching spread to the ankle and knee. Further inquiry revealed that he suffered from headaches and tenderness of the vertex of the head occasionally. He had acquired syphilis in his teens for which he was imperfectly treated (blood W.R. ++, C.S.F. 20 lymphocytes, W.R. ++, globulin present). He was energetically treated with bismuth and later with N.A.B. He recovered quite well and is now able to play football. This case must have been one of localized meningitis in the region of the motor area for the lower limb.

*Vascular manifestations.*—After a variable period, with or without prodromal symptoms, vascular thrombosis may occur. These cases are usually more acute rather than chronic. These vascular accidents tend to occur within about 18 months of infection. Syphilitic hemiplegias may not differ essentially from hemiplegias due to other causes; but in syphilitic cases it is more common for 'warnings' to be present, and often consciousness is not lost. In my series of fifty cases, eighteen came for arterial thrombosis; nine were cases of throm-

bosis of the left middle cerebral, six of the right middle cerebral, two of the anterior cerebral, and one of the posterior cerebral. The blood W.R. was positive in all these cases, but the W.R. in the C.S.F. was negative in five cases. Two of the eighteen cases died; they were very severe cases associated with definite signs of meningeal involvement. Most of the remaining cases improved quite well under anti-syphilitic treatment, but residual defects remained in all but two of the cases; in these two the impairment of function was negligible. None of the cases of left middle cerebral thrombosis regained the movements of the hand satisfactorily. They recovered their power of speech and they were able to walk.

The two cases in which the anterior cerebral arteries were involved came under observation for hemiplegia. It was only when the recovery of the movements of the upper extremity was earlier and more complete than that of the lower extremity that the anatomical localization was suspected. The case of posterior cerebral thrombosis is interesting. He was a male cook of 28 years of age, who was brought to the hospital with a history that he felt giddy and fell down the previous night. The patient was dazed but could answer questions. There was hemiparesis on the left side, and the plantar reflex was extensor on the same side. He improved very quickly and was on his legs within 24 hours. Malingering was excluded by a positive Babinski's sign. Since it is not uncommon in mild cases of subarachnoid hæmorrhage to see quick improvement, I did a lumbar puncture but found a clear C.S.F. On more detailed examination I found that he had a left-sided homonymous hemianopia. The W.R. was positive in the blood, but negative in the C.S.F.

*Latent meningo-vascular syphilis.*—It may happen that patients who come for other complaints are discovered to have some neurological signs, which on more detailed examination can be proved to be due to syphilis. The common signs observed are slight blurring of the edges of the disc, pupillary abnormalities, loss of light reflex, unequal tendon jerks and a positive Babinski's sign. There may be no symptoms attributable to the objective signs observed. I have seen two cases of this type.

*Ocular manifestations.*—Pupillary abnormalities, such as inequality and irregularity in the outline of the pupil, and loss of light reflex, are said in the textbooks to be very common; but these have been very uncommon in my experience. In fact, I have found such signs well marked in only three cases, and I have never met with a typical Argyll-Robertson pupil. Evidently such signs are less common in our parts than in England, and for this reason, they cannot be considered as very valuable signs in the detection of neuro-syphilis in India; when they are present, the diagnosis is almost certain.



As for the ophthalmoscopic appearances, I have seen no cases of optic atrophy. I have found changes in the visual fields in only four cases. All my cases that came for generalized convulsions and signs of meningeal involvement showed definite signs of slight swelling of the disc, congestion and blurring of the edges. Evidently these are due to increased intracranial pressure and involvement of the nerves at the base of the brain. Those cases which involve the optic nerve severely, giving rise to deterioration of vision, go to the ophthalmic hospitals. Whatever its limitations, I would advocate the routine use of the ophthalmoscope in all cases.

**Diagnosis.**—The manifestations of cerebral meningo-vascular syphilis are protean. They may be transient or permanent, local or diffuse, single or multiple, and any combination of symptoms is possible. Since it is the commonest cause of organic nervous disease, it should always be excluded before any other diagnosis becomes tenable. Cases of obstinate headache with neurasthenic symptoms must be investigated thoroughly. When an adult comes for fits, an organic cause must be suspected. When there are definite signs of meningitis, other causes of meningitis must be excluded. Pupillary abnormalities if present are of great diagnostic value. Whatever the clinical probability, it is indeed fortunate that serological tests come to our aid in confirming a clinical diagnosis.

**Prognosis.**—The prognosis is on the whole satisfactory, particularly when the condition is detected early and vigorous treatment is instituted. Cases with extensive arterial lesions have a bad prognosis. Cases of acute meningo-encephalitis also do not do well. The cranial nerve palsies almost always recover with anti-syphilitic treatment.

#### *Spinal syphilis (sixteen cases)*

Spinal syphilis is not really an entity by itself apart from cerebral syphilis, but the name signifies a particular anatomical localization of the infective process. The lesion may be strictly spinal without cerebral manifestations, or a combination of the two localizations may be found. In acute syphilitic meningo-myelitis, the process is usually diffuse over the meninges and the whole neuraxis. In chronic meningo-myelitis, the lesion may be localized or diffuse, and the mischief is not absolutely irreparable. It should be mentioned that the term myelitis is loosely applied; as a matter of fact, many of the observed symptoms are due to vascular mischief. Spinal syphilis may be said to give rise to various syndromes. Depending upon whether the meninges or the cord or nerve roots are more affected, the clinical picture is variable. Of my sixteen cases the types I saw were as follows:—

(1) Acute transverse myelitis ..	.. 5 cases
(2) Chronic meningo-myelitis ..	.. 6 "
(3) Spinal arterial thrombosis ..	.. 1 case

(4) Radiculitis ..	.. 3 cases
(5) Cervical pachymeningitis ..	.. 1 case

**Acute transverse myelitis.**—In this condition the inflammatory process is so violent that a flaccid paraplegia in flexion develops rapidly. In most of my cases the incubation period has been very short, three of them actually coming within a year of infection. The onset may be acute, but usually careful inquiry reveals that the patient had some disturbance of bladder function and had vague pains in the back, often radiating down the limbs. All my cases of this type were between 24 and 32 years. All of them except one were illiterate manual labourers; it is quite possible that hard manual work may have something to do with the spinal localization of the disease. The prognosis in this type of syphilis has been uniformly bad. The following case is typical.

The patient was the only literate in my cases of acute myelitis. He was 25 years old and had suffered from a sore on the genitals, for which he was treated by a native practitioner, 9 months before he came to the hospital. He had some trouble with micturition a month before he came to the hospital. The trouble was intermittent and evanescent. He suffered from pain in the back which often radiated down the limbs. He did not take much notice of it, since he attributed his troubles to heavy cycling. On the day of admission to the hospital he had ridden more than 25 miles on his bicycle. On the same evening he found that he was unable to pass urine and he came to the hospital for this reason. The retention was relieved by a catheter, but it was found that the patient was unable to move. He was admitted to the hospital. It was found that there was a complete flaccid paralysis of both the lower limbs, with abolition of all the tendon jerks. Plantar reflex was unobtainable, probably due to complete anaesthesia of the sole, and to spinal shock. The upper level of the lesion corresponded to the tenth dorsal segment, and he complained of a constricting pain around the umbilicus. Blood W.R. positive, C.S.F. W.R. positive, lymphocytes 200. No amount of treatment was of any avail, and he rapidly developed bed sores and infection of the urinary tract and died within two months of admission to the hospital.

This case is of interest in showing that there are usually many warning signs to which, unfortunately, the patient may not give heed; and it is also of interest to observe the violent physical exertion that he had before he was struck down by paralysis.

**Chronic meningo-myelitis (six cases).**—In this condition the patient usually comes for difficulty in walking. Such cases are usually referred from the out-patient department as cases of spastic paraplegia. The typical story is that they have been suffering from pain in the back, often radiating down the limbs. Associated with this it is not uncommon to get a history of disturbance of bladder function, and the libido is usually diminished. After a variable period of these complaints, which may have remissions and exacerbations, the patient finds that his legs are weak and that he is unable to walk properly. The usual signs detected are diminished power of the limbs, increased tendon jerks and a positive Babinski's sign. Slight sensory loss is common; it may often involve all



forms of sensibility, including the senses of passive position and vibration. The signs are usually bilateral, and often asymmetrical. Mild spineter disturbance is the rule. Many of these cases improve fairly well under anti-syphilitic treatment, but complete recovery cannot be expected.

*Spinal arterial thrombosis.*—In cerebral syphilis, arterial lesions give rise to definite syndromes, and it is justifiable to speak of arterial thrombosis as a definite entity. In spinal syphilis, such definite syndromes due to arterial lesions are rare. As already stated, the term myelitis is loosely applied, and arterial lesions are also responsible for parts of the clinical picture. In rare cases it happens that only one arterial branch is involved, and then it may be justifiable to use the term spinal endarteritis. I had only one such case.

The patient was a male adult of 30 years of age. His complaint was that he could not use his right lower limb properly. He was definite that the onset was sudden, though he had felt that the right leg was 'funny' a day before the final onset of weakness. On examination, the extensors of the knee were weak on the right side and there was also weakness of dorsiflexion of the ankle and toes. The knee jerk was diminished on the right side, but the ankle jerk was exaggerated. Babinski's sign was present on the right side. There were no sensory changes on the right side. On the left side, the power of the limb was good, the jerks were normal and the plantar reflex was flexor; but the sensations to pin prick and heat and cold were diminished on the left leg over its anterior aspect. The senses of position and vibration were intact. In brief, the clinical picture was like a partial Brown-Séquard. The W.R. was positive in the blood but negative in the C.S.F. This is probably a rare case of thrombosis of the lateral or sulco-marginal branch of the anterior spinal artery at about the level of the third or fourth lumbar segment. He improved quite well under anti-syphilitic treatment and all signs disappeared, save a little not easily detectable weakness of the right knee. There was, however, a definite diminution of the right knee jerk as compared with the left side. This was the only residual sign. Probably the anterior horn cells of the third or fourth lumbar segment which supply the quadriceps femoris have been permanently damaged.

*Spinal radiculitis.*—It is uncertain if this can be grouped as a separate entity, but the term can be retained for cases which come for 'root pains'. Both the anterior and posterior roots may be involved, but the sensory symptoms always precede the motor symptoms and so they come under observation for root pains. I have seen three such cases. In two of them the 5th cervical nerve was involved. In one case it was the third lumbar. These cases improve ultimately under anti-syphilitic treatment, but there is a tendency for the pains to become aggravated during the earlier phases of specific treatment, probably owing to a focal reaction. In my experience, all the cases which came for root pains had a violent exacerbation of pain after lumbar puncture; for this reason I consider that it is wise to warn the patients about a probable increase in their pain, if lumbar puncture is contemplated. All my cases had a positive Wassermann reaction in the C.S.F. The cell content was also increased moderately, 20 to 30

lymphocytes being present. [With Heilig *et al.* (1942) I have reported a case of lung syphilis with cervical radiculitis.]

*Cervical pachymeningitis.*—This is a very rare condition, which may not always be syphilitic. It is really more a panmeningitis than a pachymeningitis. The usual region affected is the cervical region. I have seen only one case of this type. The patient, an adult of 35 years, complained of pain in the neck radiating down both the shoulders and arms. He also experienced a little difficulty in walking. There was definite wasting and weakness of the muscles of the upper arm on both sides, and the biceps and supinator jerks were very much diminished on both sides. Sensory loss was indefinite. The knee and ankle jerks were exaggerated and the plantar reflex was extensor on both sides. The provisional diagnosis was one of spinal compression. The W.R. was positive in the C.S.F. and the cell count was 36 lymphocytes; there was no xanthochromia and the protein content was less than 100 milligrams. In this case also the root pains became extremely severe after lumbar puncture. I was contemplating taking a skiagram of the spine after lipiodol injection to see if there was a block, but he could not be induced to stay in the hospital and was discharged but slightly relieved.

In my series of fifty cases of meningo-vascular syphilis, the proportion of spinal syphilis has been 32 per cent. I think this is rather high as compared with England and America, where the proportion of spinal syphilis is about 20 per cent. No doubt the number of cases I have studied is small, and I am fully aware of the probable errors of statistical computation; yet I would venture my opinion that spinal meningo-vascular syphilis is more common with us than in the Anglo-Saxon races. This is indeed unfortunate, since the outlook, at least in my hands, has been more gloomy than in the cerebral cases.

*Diagnosis of spinal syphilis.*—On the whole the diagnosis is easy, since serological reactions come to our help. The condition has to be distinguished from spinal compression and disseminated sclerosis. As for the latter it is practically unknown in our parts, and I have not seen a single case of disseminated sclerosis here.

#### *Laboratory findings in meningo-vascular syphilis*

The most useful laboratory test for diagnosis of neuro-syphilis is the Wassermann reaction in the blood and cerebrospinal fluid. In addition, in this hospital, the Kahn precipitin test is also done as a routine.

*Blood.*—The shorter the incubation period, the greater is the chance of the blood W.R. being positive. Vascular cases almost always have a positive blood W.R. Some of the more chronic cases may not show a positive reaction in the blood, though the reaction in the C.S.F.,

particularly when one cubic centimetre is used, is almost always positive.

**C.S.F.**—The introduction of lumbar puncture by Quinke in 1891 is one of the most important developments in the field of neurology. The technique is quite simple, and the dangers, though not unknown, are very few, and it should be employed as a routine not only for diagnostic purposes, but also as a measure to gauge the efficacy of treatment. The fluid should be drawn slowly, and a fine needle must be used. The commonest complication is headache, which, in rare cases, can be very intractable. The post-puncture headache is probably due to a gaping puncture wound in the dura, causing constant drainage of the fluid into the epidural space. Root pains may get worse after lumbar puncture. Injudicious lumbar puncture may be dangerous in the presence of severe degrees of papilloedema.

**Pressure.**—Though I have not measured the pressure as a routine, it is customary to find an increase in the pressure of the C.S.F.

**Lymphocytosis.**—The lymphocytes are increased as a rule. The number varies greatly. As a rule the number of lymphocytes found is between 50 to 200. In meningeal inflammations, particularly if acute, both lymphocytes and polymorphonuclears are increased markedly. The more chronic the condition, the more the tendency of the cells to be lymphocytic in nature. In purely vascular syphilis, the cell count may not be increased. Under intensive anti-syphilitic treatment, the cell count decreases, and this may be taken as an index of the efficacy of treatment.

**Chemical examination : Protein.**—This is usually slightly increased. Globulin is usually increased.

**Glucose and chlorides.**—These are not sufficiently altered to be of diagnostic value.

**Lange's colloidal gold test.**—This test has not been of much value in my series of cases. Certainly, it is of great value in differentiating them from parenchymatous syphilis as in G.P.I.

**W.R. and Kahn's test.**—The W.R. and Kahn's test are usually positive in the C.S.F. They may not be positive in purely vascular cases. In such cases one has to depend upon the blood W.R.

It has been said that cases which, in spite of intensive anti-syphilitic treatment, show pleocytosis or a persistently positive Wassermann reaction, or a parietic type of response in Lange's colloidal gold test, are candidates for parenchymatous syphilis. Such cases seem to be benefited by pyrotherapy.

Regarding treatment, I do not wish to enter into details. In brief it must be realized that the treatment must be prolonged and intensive. It has been suggested that the modern methods of intensive treatment of syphilis may have something to do in the development of neuro-syphilis, either by diminishing the patients' natural powers of resistance or by causing resistant strains of the spirochæte to develop

within the nervous system. Personally, I do not share this view. In the first place there is no evidence that neuro-syphilis has increased after the advent of the arsenicals. The apparent increase in the incidence of neuro-syphilis may be due to the finer and easier methods of diagnosis which are now within the reach of the average clinician. Early intensive treatment of infected persons must necessarily decrease their infectivity, thereby diminishing the incidence of syphilis and, consequently, of neuro-syphilis. Moreover, most of my cases had not been treated for syphilis. Even in the few of my patients who have had some treatment, it has been so meagre that it cannot be considered as any treatment at all; it was not considered as a possible factor in producing neuro-syphilis. The question whether such treatment determines the development of parenchymatous syphilis or not I do not feel competent to answer.

The usual drugs used are mercury, bismuth, arsenic and potassium iodide. Though the spirochæticidal properties of mercury are undoubted, it is being rapidly replaced by bismuth. The best results are obtained by a combined therapy. I usually give weekly intravenous injections of N.A.B. alternating with weekly intramuscular injections of bismuth for 8 weeks. I do not use more than 0.45 gm. of N.A.B. since many of our patients are poorly built and do not usually tolerate a larger dose. As for bismuth, they seem to tolerate it quite well, and I usually give 0.3 gm. I have rarely seen any serious toxic reactions from bismuth. Arsenic should be used with great caution in vascular syphilis. I know of two cases treated carelessly with neosalvarsan, causing irreparable damage by violent vascular reactions.

The blood W.R. must be examined at least once in three months, and the C.S.F. must be examined in detail for pleocytosis, W.R., etc., once in six months. This will be a very valuable guide to the efficacy of treatment.

As for potassium iodide, there is no doubt as to its utility. It should be given in fairly large doses, if the patient tolerates it well. It is said that it may increase the scarring process. For this reason it is best to withhold it in cases of cranial nerve palsies until the patient is under the influence of the more definite spirochæticidal drugs such as arsenic and bismuth. I have not been able to come to any definite conclusion on this point.

From what has been stated above, it is clear that the treatment has to be very prolonged indeed. In some cases it may take years. Several courses of arsenic and bismuth may be necessary. I cannot say that I have been able to treat my cases as one ought to. It is so difficult to convince the patients of the necessity of such prolonged treatment, and they easily get tired of it. Moreover, there are the limitations of finance and the patients' own lapses. Yet there are cases which are really resistant, and in spite of several courses of arsenic and

bismuth, the serological reactions may remain positive or the C.S.F. may show pleocytosis. In such cases pyrotherapy is indicated. I usually use T.A.B. vaccine in doses of 50 to 100 millions given intravenously. In three of my patients, the W.R. in the C.S.F. became negative after four such pyrexial attacks. If, in spite of pyrotherapy, the W.R. is still positive, it is not worth while treating the patient further, for treatment makes the patient worse. Though the aim is to render patients sero-negative, it is wise to remember that it is the patient and not syphilis that we have to treat. As for marriage, eugenic and ethical advice, I do not wish to say anything; it is more easily given than followed.

#### Summary and conclusion

(1) A study of fifty cases of the various syndromes of meningo-vascular syphilis is described.

(2) Cerebrospinal syphilis is more common than parenchymatous syphilis.

(3) Spinal meningo-vascular syphilis forms a higher proportion here than in England.

(4) The latent interval seems to be very short in the vascular cases and in acute types of spinal syphilis.

(5) Most of my patients have been untreated and so it cannot be held that modern intensive

methods have favoured the development of neuro-syphilis in these cases.

(6) The comparative absence of ocular signs in my cases is pointed out.

(7) The importance of the disease to the physician, the methods of early diagnosis and treatment are briefly stated.

In conclusion, I would like to express my thanks to Dr. R. E. Heilig, First Physician of the Sri Krishnarajendra Hospital, Mysore, for the facilities given to me in preparing this paper. My thanks are also due to the doctors and technical assistants of the hospital, for their valuable and willing co-operation.

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## Medical News

### GOVERNMENT OF INDIA : PRESS NOTE

THE Government of India receive frequent inquiries as to the value and validity of certain degrees and diplomas purporting to be issued through agencies in India by the International University of Delaware (America), the Chartered University of Huron (America), the National University of Colorado, and the Charitable University of Delaware (America).

Inquiries are being made in the U.S.A. regarding the standing of these institutions. Information has so far been received to the effect that the National University of Colorado is not listed in the official directory of colleges, universities, and professional schools published by the U.S. Office of Education, nor does it appear in any list of recognized institutions with which that office is acquainted.

With regard to the 'Chartered University of Huron (America)', also known as the 'Chartered University of America', the 'National University Incorporated' and perhaps other names, the Government of India have been informed that the Federal Trade Commission, Washington, has negotiated a stipulation with this organization to cease and desist from

- (a) the use of the words 'University', 'Medical Council' or 'Board of Examinations' and such other words which may tend to create the impression that it is an institution for the promotion of learning in the U.S.A.; and
- (b) representing through the issue of diplomas, degrees, or certificates or other documents that the business of the institution is that of conducting an accredited Educational Institution and that they are recognized or accepted by any reputable college or university.

Complete copies of the stipulation are obtainable on application to the Government of India in the Department of Education, Health and Lands and if, since the

9th March, 1943, this institution has violated any of the provisions contained therein evidence of the fact should be brought to the notice of the Government of India for such further action as may be appropriate.

Investigation is still in progress with regard to the 'International University of Delaware (America)'. It appears that there is a record of incorporation in the State of Delaware of an 'International University Corporation of America'. It has been ascertained that activities of the International University Corporation of America are being directed from India.

With regard to the legal standing of such institutions it appears that in a few states in the U.S.A. legal provisions for chartering educational institutions do not preclude correspondence schools from granting degrees, and that the liberal chartering laws of some states permit the existence of correspondence schools whose practices virtually amount to the sale of diplomas and degrees. Nevertheless, degrees granted for work done wholly by correspondence are seldom if ever recognized by accredited colleges or universities or by Examining Boards of the different professions in the several states.

The Government of India wish to make it clear that they do not recognize the degrees and diplomas and other certificates or titles granted by the organizations mentioned above for any purpose whatsoever. In view of the fact that large numbers of people in India are likely to be interested in obtaining qualifications from the U.S.A., that will be generally recognized, Government feel it their duty to give the public the above information.

Certain so-called educational concerns are registered in India under the Registration of Societies Act, 1860 (XXI of 1860), and thereby it appears they tend to create the impression that they are authorized to confer educational and professional degrees or diplomas which

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# **The Principles and Practice of Tropical Medicine**

By **L. EVERARD NAPIER, C.I.E., F.R.C.P.**

DIRECTOR AND PROFESSOR OF TROPICAL MEDICINE, CALCUTTA SCHOOL  
OF TROPICAL MEDICINE, SUPERINTENDENT AND SENIOR PHYSICIAN,  
CARMICHAEL HOSPITAL FOR TROPICAL DISEASES, CALCUTTA

## **CONTENTS OF PART I**

PREFACE	Tsutsugamushi
INTRODUCTION	"Q" fever
MEASURES FOR MITIGATING THE EFFECTS OF TROPICAL CLIMATE	Typhus fever in India
DISEASES DUE TO THE DIRECT EFFECTS OF TROPICAL CLIMATE	OROYA FEVER, OR BARTONELLOSIS
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Seven-day fever of Japan	Amœbic dysentery
THE TYPHUS FEVERS	Amœbic hepatitis and liver abscess
The typhus fevers	Other protozoal and metazoal dysenteries and diarrhœas
Classical, epidemic, or louse-borne typhus	Chronic post-dysenteric ulcerative colitis
Trench fever	Sprue
Endemic, or murine, typhus	Para-sprue
Rocky Mountain spotted fever	Hill diarrhœa
	LEPROSY

The publication of this book is very timely. Normally there is a considerable demand in India for books on tropical medicine and this demand has been greatly increased by the large number of medical men coming to India from other countries. Moreover, the standard textbooks on tropical medicine have become difficult or impossible to obtain in India.

The book, however, is not merely a substitute for standard works but is an important contribution to the literature on tropical medicine. It is based very largely on the experience of Dr. Napier as Professor of Tropical Medicine in the Calcutta School of Tropical Medicine. Dr. Napier is of course known throughout the world for his work in tropical medicine and moreover he has had much help from the experienced colleagues at the Calcutta School of Tropical Medicine, and the result is a book on tropical medicine of real practical value written from first-hand experience.

The contents page of Part I is given above and it will be seen that this volume covers most of the important tropical diseases. The chapter on leprosy occupying 42 pages is by Dr. John Lowe and is entirely a new presentation of the subject.

Being an entirely new book this work will be found to be more up-to-date than other similar books. A feature of the book is the attention paid to the subject of epidemiology and to all matters connected with it. The author stresses the basic principles of tropical medicine and relates them to the known facts and to the practice of tropical medicine.

The author could not complete the book before he left India and it was decided that, to meet the immediate demand, it was advisable to publish the book in two parts. The first part, dealing with nearly all the major tropical diseases in 522 pages, is practically a complete work in itself. The second part which should be ready in a very few months will be about half the size of the first part and will include chapters on yaws, tropical ulcerative conditions, helminthic infections, diet and dietetic diseases, anemia in the tropics, snakes and snake-bite, etc.

At present the first part is being issued in a good but temporary binding of cloth-covered board. Later, when the second part is ready, the book will be available complete in one volume.

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will be generally recognized. It is therefore stated for the information of the public that the mere fact that an institution is registered in India does not imply any guarantee on the part of the Government that such concerns are so authorized.

### THE 75TH YEAR OF THE PRACTITIONER

WITH the June issue *The Practitioner* completed its seventy-fifth anniversary founded and first published by Messrs. Macmillan in 1868 under the editorship of F. E. Anstie; it has become one of the most popular and useful medical journals. It is an essentially practical publication with special emphasis on the latest information on treatment and this ideal has ever been kept by a succession of brilliant editors among whom were men like Lauder Brunton, Mitchell Bruce, Malcolm Morris and Albuthnot Lanc. Under the present distinguished editorial management, its activities have greatly expanded and it has achieved a standing never surpassed in its long period of existence. Like

many other journals *The Practitioner* has suffered owing to the war and on two occasions the journal, printed and ready for distribution to subscribers, was utterly destroyed by enemy action; yet a duplicate issue was prepared and was in the hands of subscribers before the end of the month on each occasion. We tender hearty congratulations to our contemporary on the completion of seventy-five years of service to the medical profession.

### THE MEDICAL COLLEGE MAGAZINE, BENGAL

WE have received a copy of the October issue of *The Calcutta Medical College Magazine* which is now in the eleventh year of its existence. It contains several articles, six of which are from the pen of senior medical students, and it gives in its closing pages various news of the college and of the students' union. The get-up and printing are good. The magazine should be welcome to students and ex-students of the college and we wish it success.

## Current Topics

### B.C.G. Vaccination in Montreal: Statistical Analysis of the Results of Research by Dr.

#### J. A. Baudouin on B.C.G. Vaccination in Montreal

By J. W. HOPKINS

(*American Review of Tuberculosis*, Vol. XLIII, 5, May 1941, pp. 581-599)

B.C.G. VACCINATION has had little vogue in Britain, partly because the incidence of tuberculosis on young children is relatively low (of the 25,176 deaths attributed to all forms of tuberculosis in 1938, 1,377 were at ages under five and of the 21,932 assigned to respiratory tuberculosis only 149), partly because the claims of Calmette and his disciples were extravagant and their statistical data grossly defective. But there was nothing biologically absurd in Calmette's argument, and there is room for further careful statistical analysis. The present paper is an example of such careful work. The data are not numerous, but cover some thousands of years of life, and are derived from the observation of more than two thousand children. Pains have evidently been taken to secure real comparability of controls and vaccinated children and precision of diagnosis. The result is to make it probable that in respect of both mortality and morbidity, the vaccinated children had a significant advantage over the controls; mortality rates and morbidity rates were uniformly lower; for instance, taking active tuberculosis, the morbidity rate in the controls (ages 0-5) was 120 per 1,000, in the vaccinated 31. Mortality rates were 54 per 1,000 and 19 per 1,000 respectively. Mortality rates from causes other than tuberculosis showed no significant difference between the groups.

.Reprinted from *Bulletin of Hygiene*, 16, 10, 1941.

### Historian of the I.M.S.

(From the *Lancet*, ii, 19th December, 1942, p. 733)

COLONEL D. G. CRAWFORD, who died at Ealing on 9th December, at the age of 85, has left his own memorial. Born at Chinsura in 1857, his father being a member of the Bengal civil service, he qualified at Edinburgh in 1881 and entered the I.M.S. the same year. He retired in 1911, rejoining for five further years on hospital ships during the late war. His *History of the Indian Medical Service (1600-1913)*, published in 1914,

throws many curious sidelights on old-time Anglo-Indian life, but its main purpose was to record the evolution of a homogeneous service from the small beginnings of the 17th century. True to British precedent, early mistakes were made good and utilized to achieve order and success. In Emerson's words, which Crawford was wont to quote, they builded better than they knew. Crawford's history ranks with the best of the many regimental histories of the British army, and in 1930 he completed his *Roll of the Indian Medical Service*. How he found time in the short human span to collect his knowledge and compile these rolls is easy to ask but can only be answered by those aware of the self-sacrificing devotion entailed; and Crawford found time also to be generous, for he contributed many notes about the Army Medical Service which have yet to see the light in an addition to Johnston's roll.

### Nine Lives of Status Lymphaticus

(From the *Lancet*, ii, 19th December, 1942, p. 732)

AFTER a careful pathological and statistical analysis of 600 odd cases of either sudden death in apparently healthy people or death in people of 15 years or over who had an apparently glandular thymus, Young and Turnbull in 1931 reported that they found no evidence that so-called status thymo-lymphaticus had any existence as a pathological entity, and a leader in our own columns seemed justified in announcing, without sorrow, the end of the status. A few years later Cohen agreed that 'the term status lymphaticus used in the coroner's court is a meaningless expression'. Yet three years ago Taylor reported on 14 cases in which the only explanation of death was in his view a general excess of lymphoid tissue, making it clear that it was this general excess rather than enlargement of the thymus which should be looked upon as predisposing to death from trivial causes. And now Millar and Ross have satisfied themselves that one of the other characteristics of the lymphatic state—aortic hypoplasia—is significantly associated with accidental death. In a series of autopsies in which they measured the aortic circumference at a fixed level they first eliminated aortas with well-marked atheroma, and those from obese, emaciated or oedematous patients, leaving 300 measurements for analysis, 26 being from patients dying as a result of accident. By applying multiple regression corrections, variations for height, age, weight and sex were eliminated, and it then appeared that the mean aortic circumference in the accident cases was 1.48 mm. less than in non-accident cases. From this Millar and



Ross argue that aortic hypoplasia is connected, probably indirectly, with liability to accident, and even imply a connection with 'accident proneness'. The argument is fallacious. We are told no details of the accidents, whether they were in air raid, factory or on the road. The existence of accident-proneness is well established from close observation of the precise nature of industrial accidents; without detailed study of circumstances it would not be right to connect 26 accidental deaths with accident-proneness as Newbold understands it. Technical improvement in post-mortem work is, day by day, finding causes for deaths which only 10 years ago would have been regarded as mysterious, and in the heyday of status lymphaticus would have been assigned thereto. Careful interpretations of data have elucidated deaths from functional causes like vagal inhibition, carotid and reflex, and careful technique has established the unsuspected frequency of air embolism, amniotic embolism, allergic death and the like, all missed with ease. There may well exist, as Campbell puts it, 'a condition of such lower resistance and hyper-susceptibility that the patient so affected is in danger of sudden death from trivial causes'; one feature of this condition may be a type of aorta with narrowing and hypoplasia of its wall, but the connection between the two has yet to be convincingly established. And there is always a cause of death awaiting detection.

### Cutaneous Diphtheria in Northern Palestine

By J. D. S. CAMERON, M.D. (Edin.), F.R.C.P.E.  
COLONEL, R.A.M.C.

and

E. G. MUIR, M.S. (Lond.), F.R.C.S.  
LIEUTENANT-COLONEL, R.A.M.C.

(From the *Lancet*, ii, 19th December, 1942, p. 720)

IN military operations in the Middle East during the last war, affections of the skin were a common cause of temporary inefficiency among the troops. Large numbers of men are again stationed in the same areas, and skin affections are again a major problem. One of the more common of these cutaneous affections, and one which caused considerable disability in the last war, is that known as desert sore, veldt sore or Barcoo rot. Working in the Sinai Peninsula, Craig (1919) found that in 67.5 per cent of his cases of such sores the Klebs-Löffler bacillus could be isolated. The virulence of these organisms was not determined. While not suggesting that all veldt sores are diphtherial in origin, Manson-Bahr (1941) points out that in a certain proportion this aetiology must be taken as established. Bensted (1936) published an account of an outbreak of diphtheria among British troops on the North-West Frontier. In his 46 cases there were 31 of cutaneous diphtheria, the ulcers being situated mainly on the knees, hands and arms; 5 cases showed post-diphtheritic paresis, 3 of the cutaneous and 2 of the faucial type. Good results were obtained with antitoxin. The whole battalion in which the outbreak occurred was Schick-tested and those positive (27 per cent) were treated by at least two prophylactic injections. Hamburger (1939, 1940) found virulent Klebs-Löffler bacilli in over 3 per cent of the cases of 'so-called frontier sore' which he investigated in India.

In an outbreak of diphtheria in Northern Palestine, reported by Cameron (1942), a large number of cases of cutaneous infection were noted. The unit showing the highest incidence of affection was a British Yeomanry one which had been stationed in Northern Palestine since arrival in the Middle East. During June to August 1940, faucial diphtheria broke out in the unit, 12 cases being admitted to No. 61 General Hospital. A carrier was found and after his isolation and treatment the outbreak seemed to die down. Before this outbreak, sores had been noted but they did not seem to be more numerous than in other regiments similarly situated, nor to take longer to respond to the usual local treatments. After the faucial diphtheria outbreak the sores continued to be prevalent, but now

many of them proved resistant to treatment—indeed seemed to retrogress despite it—and in several deep indolent ulcers developed; 4 of these cases were seen in the same hospital in September, when the unhealthy appearance of the granulating base and the rolled edge suggested the possibility of a diphtheritic infection. Swabs and scrapings were therefore taken from the bases of the ulcers after removal of the overlying scabs and these showed the presence of Klebs-Löffler bacilli. Other cases of apparently similar skin lesions in the unit were examined and 15 further cases were scraped, yielding 10 positive results. Later, further cases were admitted from this and other units. The condition was found to be prevalent in all parts of Palestine but was especially common in the north.

The total number of cases of cutaneous diphtheria from September to December 1940, was 66. Over this period other types of diphtheria were developing in the same units. An analysis of the outbreak showed: nasal diphtheria 26; faucial diphtheria 79; cutaneous diphtheria 66 cases; and carriers 78. All cases of cutaneous lesions underwent routine swabbing of nose and throat. Of the 66 cases, 42 were unassociated with positive findings elsewhere, while the remaining 24 showed the following lesions: faucial diphtheria 8; nasal diphtheria 4; nasal and faucial diphtheria 3; and carriers 10 (nose 3, throat 4, both 3).

#### THE SKIN LESIONS

Cutaneous diphtheria was encountered in two forms, acute and chronic. The acute form was always associated with a positive lesion of the throat, or more commonly the nose. The chronic form was invariably superimposed on a skin lesion, which might be any form of skin disease; the commonest associate by far was the desert sore, but association was often noted with scratches, insect bites, impetigo, scabies, staphylococcal folliculitis and epidermophyton, one case followed typical herpes zoster.

*Acute cutaneous diphtheria.*—The acute sore was found both on unbroken skin and at sites of previous trauma. The association with diphtheria of nose or throat probably explained why the sore was so often found on unabraded skin of the radial aspect of forearm and dorsum of hand; it was doubtless the result of direct transference through nose-wiping on the part. The first clinical sign in such cases was a small blister or pustule centred around a hair follicle; after rupture a flat shallow sore developed with base almost flush with skin and edge composed of skin only—no rolled bluish edge as in the chronic type. The base appeared more healthy than in the chronic type and in the absence of mixed infection yielded a pure growth of *Corynebacterium diphtheriae*. In one case aspiration of the pustule before it ruptured gave a similar pure growth. Where a pre-existing sore became acutely infected there was no preceding blister but the blackish membrane developed rapidly. Size, shape and depth varied with the antecedent lesion.

One case of this type calls for special mention. The initial lesion was a mosquito bite of the right upper eyelid. This broke down and spread along the lid giving a typical acute sore of the linear type; conjunctivitis was also present. Swabs from both sources and also from the nose and throat were positive for *C. diphtheriae*. The patient later developed polyneuritis; 80,000 units of diphtheria antitoxin were given in treatment over the first two days of the disease because of extreme systemic disturbance. The conjunctivitis was non-membranous.

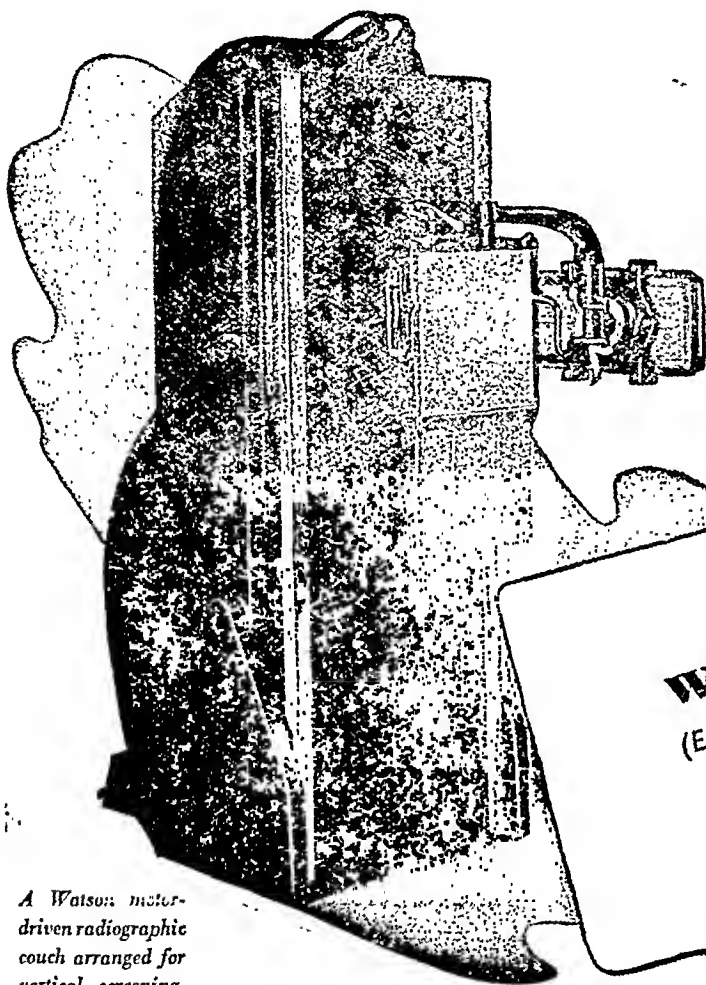
*Chronic cutaneous diphtheria.*—The sores were more commonly seen in their chronic or indolent stage. Almost invariably multiple, they were usually found on the elbows, forearms and backs of the hands, the knees, legs and ankles.

In one patient who had suffered from sores for some 2 months there were present in a healed or indolent stage 84 lesions on the arms alone. Originally small staphylococcal lesions, the majority yielded positive swabs. This case was erroneously described by Manson-Bahr (1941) as acute cutaneous diphtheria.

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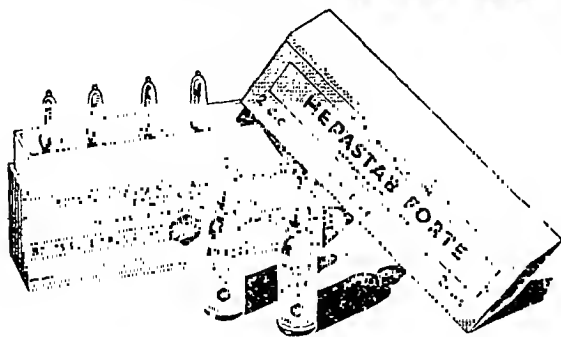


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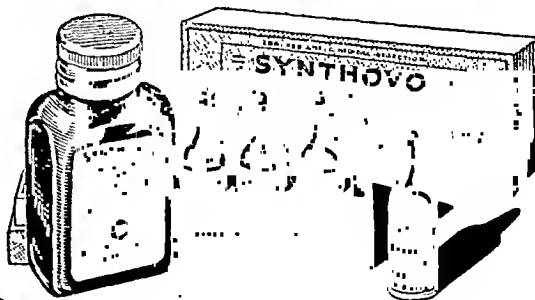
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The chronic sore was usually circular or oval, occasionally linear in an infected scratch. Punched out and clear-cut, it varied in width from 3rd inch to as much as 2 inches. The edges were hard, raised and rolled, with a pale-bluish tinge, and the base was flat and even. In many it was covered with a leather-like, dark scab membrane beneath which was unhealthy pus-containing anemic granulation tissue. From time to time this scabbed-over appearance suggested healing, but only to bring disillusionment when once again pus appeared beneath the scab. Manson-Bahr (1941) records a case where the ulcer had been present for 2 years. Enlargement of the regional lymph nodes was not common in the absence of acute pyogenic infection. Many of these sores appeared to originate in insect bites or wounds that had become infected. In one case where the patient had an ulcer with a positive smear between the third and fourth toes, an epidermophytic origin seemed probable.

Acute and chronic sores may be encountered in the same patient, the acute lesion usually being a contact infection of healthy skin from the chronic. This was well illustrated in a patient with multiple chronic sores who developed a positive acute ulcer on the right side of the scrotum exactly opposite a lesion on the right thigh. The healed acute sore left little change in the part. The chronic sore left a scar which was usually thin, glossy, brownish pigmented and slightly depressed. There was no recovery of hair or sweat glands in the scarred part.

#### DIAGNOSIS

An acute diphtheritic infection of the skin may be suspected when blister sores appear on the forearm or hand of patients suffering from active nasal or faucial diphtheria, or where, in such a case, a pre-existing skin lesion in any part of the body becomes obviously exacerbated and develops a yellowish membrane or dark leathery slough. The diagnosis can only be proved by finding the *C. diphtheriae* and establishing its virulence.

The chronic diphtheritic sore has clinical features which distinguish it from the commoner desert sore. It is oval or circular, the edge is raised, rolled and bluish while the base is deep and may show the leathery membrane slough beneath which are pus and unhealthy granulations; whereas the desert sore is more irregular in shape, lacks the raised rolled edge, and is shallow; its healthier-looking base is covered only by a thin dry light-brown scab of sero-pus which often entangles the surrounding hairs. The punched-out appearance of the diphtheritic sore and absence of healing may suggest a syphilitic ulcer but this is easily excluded by the specific tests. In areas where it occurs, cutaneous leishmaniasis may strongly resemble the diphtheritic ulcer. Examination for the Leishman-Donovan bodies in the fluid removed from around the margin of the ulcer will help to establish the diagnosis.

As in the case of the acute sore the diagnosis of the chronic diphtheritic ulcer can only be definitely established by bacteriological findings, though with experience a correct clinical diagnosis can be made in a large proportion of cases. Careful preparations are needed before taking a smear. The slough membrane must be removed, after which the sore should be treated with a saline dressing, kept moist for at least 24 hours. The sore should be freed as far as possible from antiseptic influence. The smear should be taken by scraping the surface of the sore and especially under the margins with a spoon or platinum loop, the customary cotton-wool swab being much less likely to give positive results. Direct transference to the Löffler medium is desirable. One negative finding should not upset a clinical diagnosis. In an outpatient, a spirit swab applied for half an hour may be used in place of the saline dressing.

#### BACTERIOLOGY

In the present series no case was diagnosed as diphtheria without bacteriological verification. In most of the early smears morphology and fermentation tests were regarded as sufficient evidence. Wherever doubt

existed growth on Morgan and Marshall tellurite medium was employed for verification. Later, when sufficient tellurite was available this was a routine. By this means a large number of cases with diphtheria-like organisms were excluded from the series; diphtheroids abound in skin sores, and often full bacteriological evidence is necessary before a diagnosis of cutaneous diphtheria can be established.

Virulence tests were carried out on 11 cases taken at random from those in hospital; of these, 8 were reported virulent, while one of those reported avirulent later developed polyneuritis. In this case no focus of diphtheria other than cutaneous was found. A second case with multiple infection (nose, throat and skin), though reported avirulent, later developed paralysis. The virulence test employed initially was of the intradermal type but in later tests intraperitoneal injection was carried out with a full autopsy of the animal after death. The nose and fauces were repeatedly swabbed in all cases. Nasal as well as faucial swabbing should be routine in all cases of diphtheria, especially cutaneous.

In a large number of cases a staphylococcal lesion provided the basis of the diphtheritic sore. These staphylococcal lesions were invariably multiple and included cases of folliculitis, boils and desert sores, the staphylococcus being the commonest organism associated with this last. In nearly all these cases *Staphylococcus aureus* of similar type to the skin infection was found in the nose. The coagulase test was employed by Major S. Cowan to establish the virulence of these organisms. The number of positive results justifies the suggestion that a large number of skin infections with staphylococci are of nasal origin and that in such cases a staphylococcal vaccine may be of therapeutic value.

The diphtheritic infection was thought to have its source in the native population. This point is discussed elsewhere (Cameron, 1942). The horse is exonerated as a source of infection; bacteriological examinations of horse nasal and salivary swabs, hair, curry-combings, dry and wet manure and forage were all negative. Craig (1919) ascribed the sores to horses bedded in dried manure; Bensted (1936) reported positive findings in the forage used on the North-West Frontier. It is interesting that much of the forage used in Palestine, including that tested, was of Indian origin.

#### PROGNOSIS

In all instances the acute sores healed rapidly. The chronic sores were remarkably indolent; none healed in under a fortnight after coming under hospital treatment; over a month was more usual. Most of these chronic sores had been under treatment for at least a month before admission; one case had had unhealed sores for 8 months.

Paralyses developed in 12 of the 66 cases: 2 were in cases of cutaneous diphtheria in carriers; 2 cases were associated with nasal diphtheria with the acute type of cutaneous sores; 2 were associated with both nasal and faucial diphtheria; in 5 no focus of diphtheria other than the skin could be found. Of the 66 cases, 42 were unassociated with diphtheria elsewhere; of this number 5 cases developed paralyses. Palatal paralysis was found in one case associated with nasal diphtheria and in one patient who was also a carrier; one case associated with nasal infection showed facial paralysis and one showed accommodation loss. Circulatory failure was present in one case of nasal and acute cutaneous diphtheria. Bensted (1936) reported 3 cases of paralysis in 31 cases of cutaneous diphtheria; Walshe (1918) also noted it in association with cutaneous lesions. Apart from these records, the association of paralysis with skin diphtheria does not appear to have been emphasized. The high percentage incidence makes careful antidiphtheritic treatment necessary, as in the faucial cases; it is too often unavoidably delayed until the toxin has become firmly fixed. Sensory symptoms were manifest in the vast majority of the cases of diphtheria of all types, and are therefore not included in the above analysis. The table gives detailed analysis of

the paralysis encountered. Points of note are the predominant affection of the lower limbs and the remarkable symmetry of the muscles involved. In all but one of the cases the paralysis was a late development after the sores had healed. The longest interval after initial treatment was 149 days.

#### TREATMENT

The acute ulcer required little treatment beyond that of the major causal condition and bland moist dressings to the sore. The presence of such a sore did not indicate need for any change in dosage of antidiphtheritic serum, the dose of which should be suited to the nasal or faucial lesion.

also high. No vitamin preparations were used other than routine 'marmite'. The chronic sore should be treated in bed with the part immobile as far as possible.

In view of the chance of paralysis, diphtheria antitoxin was given to all cases. Since no controls were used it cannot be said whether this assisted healing. In some cases, however, antitoxin treatment was delayed for some time pending positive diagnosis. The general impression in these cases was that healing was more rapid after the injection than before. A minimum dose of 20,000 units was given in all instances. In view of the high incidence of paralysis it is debatable if the high-dosage method of Bie (1940) would not have been

#### NATURE OF PARALYSIS IN 12 CASES

Case	Cutaneous lesion	Dose of ADS units	Loss		PARALYSIS			Circulatory disturbance	Polyneuritis	Muscles affected.
			Sensory	Reflex	Palatal	Accommodation	Facial			
1	Legs and fingers (carrier).	24,000	+	+	+	-	-	-	+	Right trapezius, serratus, quadriceps, gastrocnemius, tibialis ant. Left quadriceps, gastrocnemius, tibialis ant.
2	Right hand, acute (nasal diphtheria).	16,000	-	+	+	-	+	+	+	Right abdominals, recti, and laterals, gastrocnemius. Left abdominals, recti.; ileopsoas; gastrocnemius; tibialis ant.
3	Toe, acute (nasal diphtheria).	40,000	+	+	-	-	..	-	+	Left-sided paralysis with hemiplegic distribution of lower neurone type.
4	Feet (carrier) ..	20,000	-	+	-	-	..	-	+	Arms free; bilateral quadriceps weakness.
5	Legs and arms ..	20,000	-	-	-	+	..	-	-	No demonstrable motor weakness except of accommodation.
6	Heel ..	22,000	-	+	-	..	..	-	-	Reflex loss with no demonstrable motor weakness.
7	Hands and knees	24,000	+	+	-	..	..	-	+	Lower limb weakness especially in both quadriceps.
8	Arms ..	20,000	+	+	-	..	..	-	-	No demonstrable motor loss; deep reflexes absent on both sides.
9	Left ankle. Right leg.	20,000	+	+	..	..	..	..	+	Weakness in left forearm and both lower limbs notably quadriceps.
10	Foot (epidermophyton).	32,000	+	+	-	..	..	-	+	All muscles of lower limbs with quadriceps +++.
11	Forearm, nose, throat and ear.	32,000	+	-	-	..	..	-	-	Sensory only.
12	Right upper eyelid, conjunctivitis (nose and throat diphtheria).	80,000	+	+	..	..	..	..	+	Right gluteus maximus and medius, quadriceps, hamstrings, gastrocnemius, tibialis ant., peroneus longus, toe flexors. Left as for right with peroneus brevis in addition.

Treatment of the chronic ulcer fell under two heads—general and local. Cutaneous lesions are undoubtedly common in the Middle East and take considerably longer to heal than at home. The climate, excessive exposure of skin to sun, the lack of fresh fruit at certain seasons, the increased tendency to abrasions in certain occupations such as grooming, the difficulty of keeping scratches and bites covered, clean and moist, and the attacks of insects all play their part. Consequently any factor which raises the patient's resistance to infection is important. Though the suggestion of vitamin C lack was not supported by intradermal dichlorophenolindophenol tests carried out on a number of the cases and though there were no clinical evidences of other vitamin deficiencies all cases were placed on a diet of high vitamin content. To maintain resistance also a high protein intake was given. Sodium chloride intake was

justified. Probably the long duration of the condition before treatment, with resultant fixation of toxin, would have made even such large doses ineffective. Apart from that, antitoxin was not available in such amounts, and in any case such a high incidence of paralysis was never anticipated. Antitoxin was given intramuscularly in most cases. Manson-Bahr (1941) advises the use of antitoxin (dose 4,000 units) in all cases of chronic desert sore and suggests that it should be given subcutaneously around the sore. This method was practised in a few cases with multiple sores, but larger doses (20,000 units) were injected. No beneficial result was noted from this method; the injected sores did not heal quicker than those, on the same patient, left uninjected. Swabs soaked in antitoxin were employed as dressings on some sores in patients with multiple affection. Again no beneficial effect was observed. In

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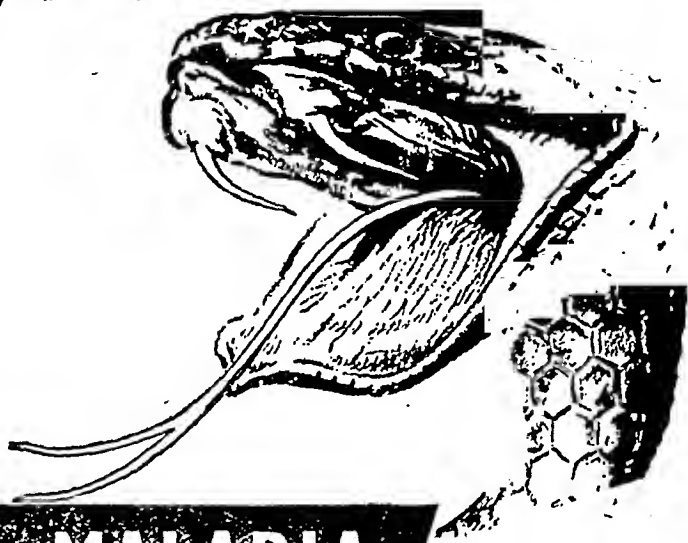
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these cases the intramuscular injection was also given.

Oral sulphanilamide and sulphapyridine were given to some cases without apparent benefit. In one case fresh sores appeared while he was under treatment with sulphapyridine. Vaccine therapy was given a trial in staphylococcal cases, as noted above.

The essentials of local treatment are that the sore should be cleaned, extensions to hair follicles with formation of satellite sores should be prevented, and healing should be stimulated and reinfection opposed. The sores were commonly in a dried, dirty condition when first seen, with scab or slough covering the base. The initial dressings should aim at removing the slough and cleaning the base. For this purpose hot fomentations, applications of magnesium sulphate in glycerine, compresses of hypertonic saline or sodium sulphate and hydrogen peroxide were all suitable measures. The surrounding hairs were removed and care was taken to prevent the dressings overlapping to allow discharge from the sore to flow over and infect the surrounding skin. A dressing cut to fit into the sore is an important point in treatment. Once the sore is reasonably clean there are two possible lines of treatment. It may be covered with plaster or strapping and left for several days or weeks. This has the advantages that the dressings are not frequently pulled off with damage to granulations, and that reinfection is prevented. But not all skins will tolerate strapping. Where the sore is small, applications of the silver nitrate stick or painting with 10 per cent silver nitrate solution will produce a black slough beneath which healing can take place. Both methods were practised with some success. In general the best results were obtained by the use of dressings which did not stick to the sore. Cod-liver oil dressings under jaconette for three days, followed by the application of scarlet red ointment for a similar period was the treatment most used. In the later stages all of the aniline dyes were used and proved efficacious. Sulphanilamide and sulphapyridine were used locally in some cases, but the rate of healing of sores so treated showed no improvement on that of control sores in the same patient treated by the above methods.

It is unwise to bind oneself to one form of treatment; whatever is done, any large diphtheritic sore is likely to take 3 to 4 weeks to heal.

We wish to thank Colonel D. Stewart and his staff, Colonel J. Higgins and his staff, especially Lieut.-Colonel C. R. Christian, Major S. Cowan and Major R. D. Mackenzie for their help with the pathology studies; the commanding officers and regimental medical officers of the regiments involved; and Captain E. L. Manton for the photographs.

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### Bacteriological Diagnosis of Typhoid Fever by Bone-Marrow Culture

By I. G. ITSKOVITCH

(Abstracted in the *Bulletin of Hygiene*, Vol. XVII, September 1942, p. 618 from the *Trans. Kuibyshev Milit. Med. Acad. Red Army*, Vol. IV, 1940, p. 141)

CULTURES of the bone marrow were employed as a method of diagnosis of typhoid fever in 56 cases, of which 42 were at the height of the disease, 9 in the state of defervescence, and 5 convalescent, their ages ranging from 2½ to 65 years.

Material for culture was obtained by sternal puncture (Arinkin's method). From 0.5 to 1 c.c. of the punctate was first inoculated into tubes with 5 c.c. bile broth, and after 18 to 24 hours subinoculated on a neutral agar slope, on which there was usually good growth on the following day. The organisms were identified by the methods usually employed for the typhoid group. As controls, simultaneous blood cultures were taken in 51 cases. The results were positive in 49 per cent of blood cultures and in 90.2 per cent of myelocultures, thus proving the superiority of the latter as a diagnostic method. It was shown to be especially valuable in cases examined late in the course of the disease (*in statu decrementi*). While blood cultures taken from such patients are always negative, cultures of the bone marrow have grown well in 88.8 per cent of cases. However, no growth was obtained in cultures from convalescents.

### A Preliminary Report on the Treatment of Bacillary Dysentery with Succinyl Sulphathiazole

By E. J. POTH

B. M. CHENOWETH

and

F. L. KNOTTS

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXVIII, November 1942, p. 162)

WHILE the results of treating bacillary dysentery with the sulphonamides are so good in the United States, it must be realized that this outcome is partly due to the excellent state of nutrition usually encountered here. In areas where states of poor nutrition exist, especially among children, mere bacteriostasis does not give such brilliant results, because the diarrhoeas of the specific bacillary dysenteries are complicated by malnutrition. Under these circumstances attention to general care, fluid, and electrolyte replacement, and nutrition must be held of equal importance with specific drug therapy.

Under ordinary conditions of our national civilization, sanitary safeguards and food protection are developed to a high degree and bacillary dysentery among adults is not a serious problem. In the armed forces, however, men in strange climates and frequently in insanitary surroundings are unduly exposed, and infection of the adult becomes a problem of major importance. Because of the apparent great efficacy of succinyl sulphathiazole in bacillary dysentery and the absence of toxic symptoms due to the administration of this drug, it would be highly desirable to consider the use of succinyl sulphathiazole as a prophylactic agent. A small quantity of drug given in the daily ration of men in areas of heavy exposure might offer protection. Such a protective dose might be surprisingly small; and in the absence of any effect on the sensorium, as determined by reaction time, and so on, the drug could be administered to great advantage.

The doses given in the cases of bacillary dysentery reported here may well be much larger than is required. No toxicity to the drug has been observed in any of these patients, and there were no instances where the drug failed to arrest the disease in a very short time. Since the minimum effective therapeutic dose of succinyl sulphathiazole has obviously not been established, a satisfactory prophylactic dose might be surprisingly small.

Because sulphathiazole is highly effective in bacillary dysentery, because the activity of succinyl sulphathiazole is probably due to the degradation product, nascent sulphathiazole, and because succinyl sulphathiazole can be maintained in high concentration in the bowel with only slight absorption and without the development of toxic manifestations, it is not surprising that succinyl sulphathiazole in tolerated therapeutic

doses should have a pronounced antibacterial activity against the organisms of bacillary dysentery. In all fairness it should be stated that during the past summer bacillary dysentery was not prevalent, and the disease might have been relatively mild. This communication should, therefore, be regarded as a preliminary report. Kirby and Rantz have, however, succeeded in curing bacillary dysentery carriers with succinyl sulphathiazole.

#### SUMMARY

The treatment of bacillary dysentery with a new chemotherapeutic agent, succinyl sulphathiazole, is presented. The drug is equally effective in both the acute and the more chronic forms of the disease. All cases of bacillary dysentery treated responded promptly. The administration of the drug caused no untoward toxic manifestations.

### Trypanosomiasis treated with 'Pentamidine'

By T. L. LAWSON, M.B., D.T.M. & H.

(Abstracted from the *Lancet*, ii, 24th October, 1942, p. 480)

THE following facts are to the credit of pentamidine. It produces a rapid peripheral sterilization of the blood and gland juice.

Treatment is complete in 10 days instead of 10 weeks, as with other drugs available; this is extremely important from the point of view of the patient and for the preventive medical aspect.

Toxicity is low, especially in comparison with trypanamide (which is responsible for many cases of blindness in Africa). The effective dose is not more than half the toxic dose and probably almost a fifth the lethal dose.

On the debit side are its lack of success when the examination of the CSF shows serious CNS involvement. When the cell count in the CSF is above 80 per c.mm., it is probably safer to use one of the pentavalent arsenicals. Some cases with counts above that figure were cured, but others were not.

It is not safe to base too much reliance on the analysis of a mere 53 cases, but it does seem that this is probably the best drug so far produced for the early cases of sleeping sickness. If it is used, however, lumbar puncture should be done in all cases, and no case with a CSF cell count of 80 per c.mm. or more should be given pentamidine unless it can be carefully followed up. Control differential white-cell counts during treatment are advisable but not absolutely essential if dosage is reasonable. It is not practicable to give exact dosage per lb. of body-weight of the patient, since in Africa treatment is often in the hands of people who cannot calculate such niceties. Our rough method probably suffices in all but the most civilized surroundings.

### Treatment of Pernicious Anaemia with an Experimental Proteolysed Liver Preparation: Preliminary Observations

By L. J. DAVIS, M.D., F.A.C.P. (Edin.), M.R.C.P.

L. S. P. DAVIDSON, M.D., F.A.C.P. (Edin. and Lond.)

D. RIDING, M.D., M.A.C.P.

and  
G. E. SHAW, B.Sc., Dip.Bact.

(From the *British Medical Journal*, i, 29th May, 1943, p. 655)

THE treatment of pernicious anaemia by parenteral injections of liver extracts has almost universally replaced the oral administration of whole liver. Among the disadvantages of whole liver are its relatively high cost, the difficulty of ensuring a regular supply, the distaste engendered by its prolonged administration,

and the uncertainties attending its assimilation in patients whose digestive and absorptive processes are impaired. Recent reports, however, have indicated the superiority of whole liver in the treatment of certain types of macrocytic anaemia, such as those occurring in pregnancy, sprue, and tropical nutritional deficiency states; occasionally cases of these anaemias have in fact been shown to be refractory to fractionated liver extracts administered parenterally but amenable to whole liver given by mouth. Accordingly it occurred to one of us (D. R.) that it might be an advantage to administer to such patients whole liver in a soluble predigested form.

#### 'PROTEOLYSED LIVER'

In the normal physiological process of assimilation of whole liver, absorption presumably begins as soon as any soluble split products are formed as the result of acid peptic digestion and alkaline tryptic digestion. In view of the impossibility of reproducing these processes exactly in the laboratory it was decided to attempt the experimental preparation of predigested whole liver. Papain was chosen as a suitable enzyme for use, since this will react at the natural pH of minced liver—namely, approximately pH 5.6. In this way the danger of the destruction of active principles by exposure to acid or alkaline conditions would be avoided.

*Process of preparation.*—Take 330 lb. of minced liver in a steam-heated pan. Add 36 gallons of water and 660 g. of papain, and heat the mixture to 60°C. Maintain the temperature at this level for three hours. Then raise the temperature to 100°C. and boil vigorously for ten minutes. Strain the hot digestion mixture through cloth, and concentrate the filtrate at a low temperature in a vacuum still to 20 gallons. Clarify the concentrate by filtration, using sterilized kieselguhr as a filter aid, and then sterilize by filtration through suitable asbestos pads. Dry the sterile liquid in a low-temperature vacuum oven.

*Properties.*—The product thus obtained is a dry, sterile, granular light-brown powder which is not unreasonably hygroscopic. It is completely soluble in hot or cold water, giving a solution that is reasonably palatable, being free from the characteristic liver flavour. It seems probable that as the cell walls are disrupted a high proportion of the water-soluble constituents will be liberated and hence retained in the final product, and that any active principle initially present as a protein complex will be set free and so be rendered available for immediate absorption. In proteolysed liver there is present predigested protein material in addition to essential haemopoietic factors. Fats, fat-soluble vitamins, and coarse indigestible material are alone discarded. It is estimated that one ounce of proteolysed liver powder is derived from approximately six ounces of raw 'wet' liver, after allowing for losses due to the mechanical process. A chemical analysis gave the following data:

Loss at 100°C.	Copper	.. 0.003%
(moisture) .. 6.2%	Iron	.. 0.04%
Nitrogen .. 12.7%	pH	.. 4.95
Ash .. 5.8%		

Preliminary tests indicate that riboflavin is present in a concentration of 10 mg. per 100 g., as determined by the method of Shaw (1939).

Thanks to Dr. Bullock of Manchester University, it has been possible to spray dry the sterile liquor, and thereby obtain an even more satisfactory product.

#### CLINICAL TRIALS

The suggestion that proteolysed liver may prove of value in the treatment of certain macrocytic anaemias refractory to the usual liver extracts renders it desirable that the efficacy of this preparation should first be determined in the treatment of the much commoner and more readily available cases of classical Addisonian pernicious anaemia. The object of the remainder of this communication is therefore to record the results obtained in the treatment of five such cases.

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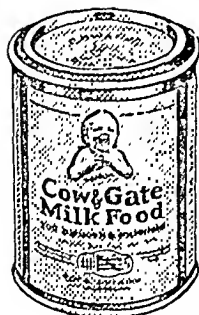
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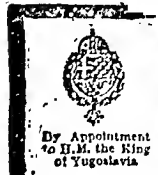
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All the patients were typical examples of pernicious anæmia in relapse as regards both their clinical and their hæmatological features. Four of them had received no liver therapy before admission to hospital. The other patient (case 4) had been treated for pernicious anæmia seven years previously, but had received no treatment during recent years. In all cases examination revealed a macrocytic hyperchromic anæmia with marked anisocytosis and poikilocytosis, and sternal puncture showed a cellular megaloblastic marrow. A histamine-fast achlorhydria was also present in all cases.

As soon as the diagnostic investigations had been completed, treatment with proteolysed liver was instituted. No other hæmatinic substance was administered during the stay in hospital. The liver preparation is in the form of a granular powder readily soluble in water. For administration it was dissolved in warm but not boiling water, pepper and salt being added to taste, making a beverage which was found by the patients to be quite palatable. The dosage given varied from two to eight teaspoonfuls of the powder daily, equivalent by weight to two drachms and one ounce respectively. The preparation was conveniently given twice daily. Arrangements have been made for the patients to continue taking proteolysed liver in a daily dose of one teaspoonful on their discharge from hospital, and they are being closely observed as outpatients. The present communication is necessarily concerned only with the therapeutic results observed during the period of treatment in hospital.

Without exception a satisfactory response was noted within a few days of the institution of treatment. In one case (case 5) reliable reticulocyte counts were not available, but the progressive improvement in her blood picture left no doubt concerning the effect of treatment. The other four patients all displayed a significant reticulocyte response, which was followed by a progressive amelioration of their clinical and hæmatological conditions.

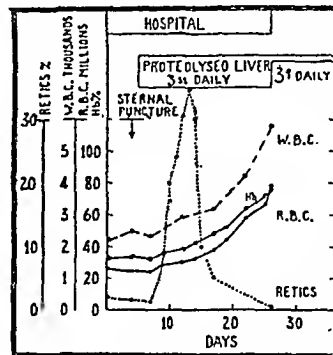
The salient features of the cases are displayed for the sake of brevity in the accompanying table, in which are set out the blood counts before treatment and on discharge from hospital, the time and degree of the observed reticulocyte responses, the duration of treatment, and the dosage employed.

*Summary of results of oral administration of proteolysed liver in 5 typical cases of Addisonian pernicious anæmia. (These data are relevant only to the period of treatment in hospital)*

* Blood counts	Case 1, aged 72	Case 2, aged 50	Case 3, aged 60	Case 4, aged 51	Case 5, aged 44
Hb .. .. . a	23%	32%	35%	44%	50%
" R.B.C. (millions): .. .. . b	61%	75%	75%	80%	83%
a	0.88	1.28	1.37	1.71	1.84
b	2.85	3.88	3.70	3.86	3.54
Rise during first 2 weeks of treatment ..	1.08	0.92	1.01	0.57	1.11
Colour index :					
a	1.30	1.25	1.28	1.30	1.36
b	1.07	0.97	1.01	1.04	1.17
W.B.C.:					
a	..	2,200	2,500	2,200	4,000
b	..	5,800	7,800	4,800	5,400
Reticulocytes :					
Maximum response .. .. .	35%	35%	17%	22%	..
Time of maximum response .. .. .	9th day	8th day	7th day	12th day	..
Time of commencement of response .. .. .	4th day	4th day	4th day	5th day	..
Duration of treatment .. .. .	34 days	21 days	29 days	20 days	20 days
Dosage daily .. .. .	3j	3ss	3ij	3ij	3ij

\* Under this heading 'a' refers to the count before starting treatment, while 'b' refers to the final count before discharge from hospital.

The average rise in red cells per c.mm. was 0.94 million during the first two weeks and 1.74 millions during the first three weeks of treatment. As regards



Graph showing response to treatment with oral proteolysed liver in a case of pernicious anæmia (case 2).

dosage, an adequate daily dose appears to be two drachms, but in certain resistant cases it is possible that a larger amount may be desirable. It should be noted that this amount is derived from less than two ounces of raw liver. Since half a pound of raw liver is the usual minimal daily quantity necessary to produce a satisfactory response in pernicious anæmia, it would seem that proteolysed liver is relatively much more effective.

Details of one typical example are given herewith.

#### ILLUSTRATIVE CASE

The patient, a married woman, aged 50 (case 2 of table), gave a history of pallor, increasing breathlessness on exertion, palpitations, nausea, and flatulence of several months' duration. Latterly she had also complained of a sore tongue and tingling of her extremities. Physical examination revealed marked pallor with slight icterus. Nutrition was slightly below standard. The tongue was atrophic. The liver and spleen were slightly enlarged. No enlargement of lymph glands was noted. No evidence of purpura was seen.



**Laboratory examination.**—Icteric index, 25; gastric analysis—histamine-fast achlorhydria; Wassermann reaction negative; sternal puncture—cellular megaloblastic marrow with some maturation arrest of the granulocytes. Peripheral blood examination showed a picture typical of pernicious anaemia in the stage of relapse. Further details of blood counts are shown in the accompanying graph.

**Treatment.**—Proteolysed liver extract was given orally in daily doses of one tablespoonful.

The patient was discharged from hospital 21 days after admission with a great improvement in her physical condition and a gain of 2.6 million red cells per c.mm. She was instructed to continue taking proteolysed liver, one teaspoonful daily.

### DISCUSSION

It is not our purpose to advocate the routine use of proteolysed liver in the treatment or maintenance of classical cases of pernicious anaemia. In such cases the existing practice of parenteral injection of reliable liver extracts is economical and effective, and in maintenance treatment has the advantage of assuring that the patient actually receives a known amount of liver extract regularly.

A consideration of obvious importance is that of cost. If it should prove practicable to market proteolysed liver at a price that will enable the cost of treatment with it to compare favourably with existing parenteral therapy, the former preparation would have advantages in the treatment of certain classes of patients—namely, those who may be situated in circumstances rendering regular injections inconvenient, those who object to injections, and those who are allergic to liver extracts injected parenterally.

It is in the field of refractory anaemias, however, that this preparation may find its most valuable application. These anaemias include cases idiopathic in origin, cases associated with pregnancy and the puerperium, and those resulting from nutritional disorders such as sprue. Although a study of the literature may lead to the conclusion that these refractory anaemias are extremely rare in temperate climates, our own experience during recent years has led to a contrary opinion.

Personal observations in support of this suggestion have recently been made on three such cases of refractory megaloblastic anaemia of idiopathic origin, which are responding to oral administration of proteolysed liver. The details of these cases are not now submitted, as it is felt desirable to continue their observation for a longer period and to await the opportunity of studying additional cases.

It is also possible that various factors present in proteolysed liver additional to the liver principle of Castle may render this preparation of value in the treatment of certain anaemias associated with a normoblastic bone marrow.

### SUMMARY

A method is described for the production of a palatable and readily assimilable whole-liver preparation by means of enzyme digestion of raw liver with papain.

The name 'proteolysed liver' is proposed for the resultant product.

Proteolysed liver administered orally has proved effective in the treatment of five cases of Addisonian pernicious anaemia.

The possible value of proteolysed liver in the treatment of classical pernicious anaemia and of refractory megaloblastic anaemias is discussed.

[Note.—It is necessary to state that proteolysed liver is not at present available commercially.]

Our thanks are due to Prof. D. M. Dunlop for allowing us to use two patients under his care for the purpose of this investigation.

### REFERENCE

SHAW, G. E. (1939) .. *Quart. J. Pharm. and Pharmacol.*, 12, 541.

## Trichlorethylene Anaesthesia

By JOHN ELAM

(From the *Lancet*, 12th September, 1942, p. 309)

IN June 1941, Hewer and Hadfield published a preliminary report on the use of a purified form of trichlorethylene known as trilene (ICI) as an anæsthetic agent; these investigators found the drug satisfactory. A further report was read at the Royal Society of Medicine on 6th March, 1942, by Hewer. Since the first report I have used trilene, or supervised its use, in over a thousand cases. Trilene is a very heavy liquid vaporizing much more slowly than chloroform or ether. It is non-irritating and non-inflammable; it has a smell not unlike that of chloroform. It is now coloured blue to distinguish it from chloroform, which is often coloured red.

Certain mysterious deaths have taken place among industrial workers who have to use trichlorethylene; it is thought that these were due to impurities. The post-mortem reports of two recent deaths in industry were unsatisfactory and no real explanation was given of their cause. Some workers in trichlorethylene are considered to be liable to splastic anaemia. Whatever the cause of recorded deaths, no anxiety as to the patient's safety has been experienced in the 1,000 administrations under review.

Trilene dropped on an open mask does not give a satisfactory anaesthesia because it vaporizes too slowly but if it is placed in the chloroform bottle of a Boyle's machine and given in conjunction with gas and oxygen a satisfactory light anaesthesia is obtained. Marrett, at the RSM in March, showed an inhaler which he had devised by which air was inspired by the patient through a bottle containing trilene. Trilene may also be given from a Shipway apparatus. The anaesthesia obtained is in some ways like that obtained with chloroform except that full muscular relaxation is not uniform.

The similar composition of trichlorethylene and chloroform led to the fear that the new drug might have similar dangers, but so far this has not been the case. There has been no evidence of primary cardiac failure during induction with trilene, there appears to be no danger from its readministration and there has been no evidence of delayed trilene poisoning.

The main features of the drug have been these. It is very easy to administer and is particularly suitable for general practitioner's work. Its administration over a long period appeared to cause no shock. (The longest administration in this series was 4½ hours.) There is very little vomiting even after long administration. For operations such as amputation of the breast there is much less hæmorrhage than when ether is used. The respiration rate increases considerably after the administration has been in progress a few minutes, but if morphia or a barbiturate is given as premedication this rise is not so noticeable and in many cases is absent altogether.

For major abdominal operation trilene alone does not give sufficient muscular relaxation, but it is very useful in the induction period, gas-oxygen-trilene being used and ether added to obtain the required relaxation.

I would especially call attention to its use in midwifery for it appears to have very little effect on the uterine muscle and a weak mixture of trilene and air will give an analgesia similar to that obtained with gas and oxygen. Other operations in this series in which trilene has been found most satisfactory have been: operations on the skull such as depressed fractures (the patients were bad risk cases, but gave no anxiety whatever), operations on the nose and throat, and dental operations. Trilene gives enough relaxation of the jaw muscles to enable a large gag to be inserted for tonsil or mouth operations. It is a great comfort to both surgeon and anaesthetist to work with a non-inflammable anæsthetic, which does away with the risk of fire of explosion from lights, cauteries or suckers. Because of its property of not increasing hæmorrhage trilene made operations on the thyroid easier, and the

# HEPOL L.Y.H.

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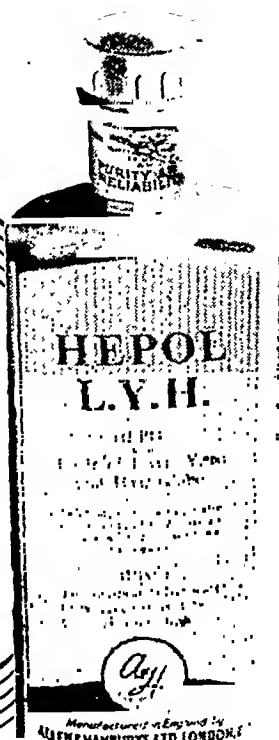
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*Descriptive literature will be sent on request.*



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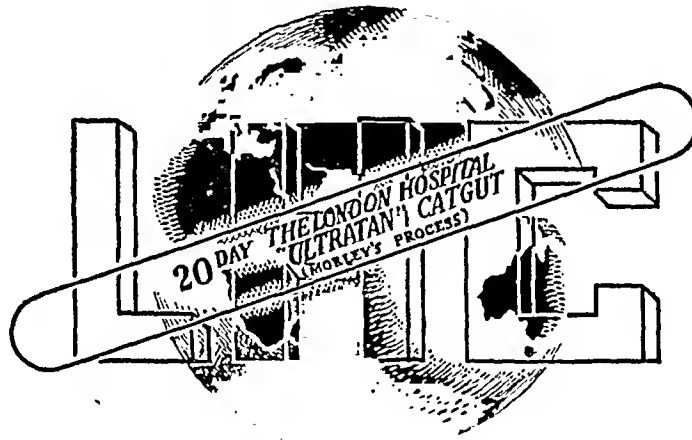
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absence of vomiting afterwards was a comfort to the patients. No attempt has been made to use trilene for intrathoracic surgery, although it has been successful for opening and drainage of empyema. It is always difficult to anaesthetize an empyema patient with gas-oxygen only, unless he has been carefully premedicated, and one is often asked to give these anaesthetics as an emergency. For orthopaedic operations especially on aged subjects—for example, the insertion of a Smith-Petersen pin—and gas-oxygen-trilene is particularly suitable.

With the Boyle's apparatus in use at most hospitals to-day it is difficult to give pure gas and oxygen anaesthesia to the resistant patient and to keep him a good colour. The addition of trilene to the gas and oxygen makes just the required difference and does not appear to upset the patient. There are very real dangers in trying to do too much with gas and oxygen, as American anaesthetists have shown and trilene seems to be

the drug we have been looking for to enable us to avoid these dangers.

Manufacture presents no difficulties, though the supply is limited at present because such large quantities of trichlorethylene are being used in industry.

#### SUMMARY

Trichlorethylene, or trilene, has been used as an anaesthetic in over 1,000 cases. There have been no deaths which could be attributed to the anaesthetic. Its non-inflammability, ease of administration and absence of postanesthetic vomiting make it a satisfactory anaesthetic when full abdominal relaxation is not required.

It is useful in conjunction with gas and oxygen for increasing the depth of anaesthesia.

About half the cases in this series were anaesthetized by medical students, to whom I am indebted for their help.

## Reviews

**ENCEPHALITIS—A CLINICAL STUDY.**—By J. B. Neal, A.B., M.D., Sc.D., F.A.C.P. 1942. H. K. Lewis and Company, Limited, London. Pp. xviii plus 563. Illustrated. Price, 42s.

DR. JOSEPHINE B. NEAL has put upon record the work of thirteen years (1927—1940) devoted to the study of a disease variable in its manifestations and tragic in its immediate and remote sequences.

The thoroughness and length of view of the band of investigators who have worked in this time with Dr. Neal is shown by the fact that the first two of these years were devoted to the collecting of the published data upon the epidemiology, aetiology and treatment of Encephalitis.

This study was published as a survey in 1929 and the practice of reviewing having been continued in further surveys appearing in 1932 and 1939.

In all 710 cases were watched (the great majority for over 5 years) by Dr. Neal who thus has an unrivalled experience of the disease.

The present work consists of chapters by the collaborators upon the epidemiology of Encephalitis, its clinical course, pathology, psychological and physiological sequelae and treatment.

It is clearly and attractively written but would have gained by a more systematic arrangement of subject-matter and greater attention to a comparison with the allied virus disease Poliomyelitis.

It is the more welcome at present when it is remembered that this grave disease first arose in epidemic form in the Balkans and the poverty and malnutrition of the last war. If these were factors in its appearance we may see it again under the far worse conditions of to-day.

Its publication is therefore most timely.

C. S.

**'PAIN.'**—By Sir Thomas Lewis, M.D., F.R.S. 1942. The Macmillan Company, New York and London

THE most important, because the commonest, symptom of disease is pain.

Sir Thomas Lewis has, in this monograph, taken up the consideration of this symptom.

His approach in that it is largely from the physiological and experimental angle, differs from that of the much larger and earlier work by Behan which bears the same title.

This subject has for over half a century fascinated many observers from Ross, Lennander, Head and Mackenzie to Hurst and Morley, and in his review

of ideas upon the mechanism of pain Sir Thomas has done justice to these and has described the views and findings of modern workers of which he himself is in many respects the most authoritative.

Perhaps the most interesting chapter is that upon the referred pain of visceral disease which has been the subject of many articles and a number of books.

Here the author exhibits his gift of lucid expression and just appraisal in a subject upon which it is more than usually hard to avoid confusion.

This is a clear exposition of a difficult and important subject and it merits careful reading by all who are interested in the meaning of symptoms, that is by all serious medical men.

C. S.

**DISEASES OF METABOLISM: DETAILED METHODS OF DIAGNOSIS AND TREATMENT: A TEXT FOR THE PRACTITIONER.**—Edited by Garfield G. Duncan, M.D. 1942. W. B. Saunders Company, Philadelphia and London. Pp. xvi plus 985. Fully illustrated including 7 plates in colour. Price, \$12.00. London price, 60s.

METABOLISM encroaches upon other fields of medicine such as nutrition, endocrinology and hæmatology, and this has presented the editor with the difficult problem of deciding to what degree these related subjects should be discussed in a work upon metabolism.

Clearly nutrition and the diseases of nutrition—the deficiency diseases—had to be included and this has entailed a review of our present knowledge of the vitamins.

Diseases of the blood have their nutritional and metabolic aspects and have received adequate mention.

Whilst it would have been out of place to have considered the endocrines in detail, these have been treated where anabolic or katabolic changes are striking as in the pituitary disorders and diabetes which has been most ably and clearly reviewed.

These chapters are preceded by the opening chapters of the book which deal fully and in turn with the metabolism of the carbohydrates, proteins, fats and minerals.

Their value lies in the link they provide for the physician between physiology and the symptoms of disease.

This massive, authoritative and valuable volume should prove to be a welcome addition to the physician's library.

C. S.

**BIOCHEMISTRY FOR MEDICAL STUDENTS.**—By W. V. Thorpe, M.A. (Cantab.), Ph.D. (Lond.). Third Edition. 1943. J. and A. Churchill Limited, London. Pp. viii plus 476, with 39 illustrations. Price, 16s.

THIS is a good book on physiological chemistry which starts with a detailed account of the elements found in the living organisms and then proceeds to consider the inorganic and organic compounds associated with life. The book appears to us to be admirably suitable for students, particularly medical students, who will find the book to be a complementary to the standard textbooks of biochemistry which he has to study. A considerable amount of new material has also been incorporated in the present edition thus making it up-to-date, well arranged and well set-up.

In view of their importance in medical diagnosis prominence has been given to the studies in relation to blood, urine and faeces. Special attention has also been paid to the principles of nutrition, digestion and absorption of foodstuffs and the metabolism from the biochemist's point of view.

The book has been written in an excellent style and the author has comprehensively dealt with the fundamental processes going on in the human body, avoiding lengthy discussions on debated points, which are often confusing to the students.

We are of opinion that the book is a valuable contribution to our up-to-date knowledge of the physiological principles in medical practice and should prove to be useful to those for whom it is intended.

J. P. B.

**THE OPHTHALMIC PRESCRIBER'S CODEX.**—By Francis E. Preston, D.O.M.S. 1943. H. K. Lewis and Company, Limited, London. Pp. vi plus 176. Price, 10s. 6d.

THIS little book of 176 pages is written for the modern ophthalmologist to make himself familiar with all the old and new remedies which should comprise his armament and to facilitate the work of reference. It is a summary of the practice of others and there is not much in it that is original. Its contents comprise three sections, the first the formulas, the second 'abridged treatment' and finally a miscellaneous section.

A detailed account is given of all the formulas used in ophthalmic treatment but many could be omitted as being unnecessary. Although all ophthalmologists would not agree with some of the methods laid down in 'abridged treatment' the advice is eminently practical and orthodox. The miscellaneous section gives much valuable advice and discusses the dangerous drugs acts; weights and measures equivalents; solubilities; vitamin contents of various foods; doses; drugs liable to be associated with idiosyncrasy; local anaesthetics, miotics and mydriatics; English and Latin abbreviations, synonyms and a glossary; normal values for cerebrospinal fluid and blood, microscopic examination of bacteria, stains, and urine analysis; the sulphonamides; electro-therapeutic adjuvants; and application of leeches, cauterization of an ulcer and hot baths. Considering the book has to comply with the authorized economy standards, it is well brought out and can be purchased at a reasonable cost. On the whole the book is excellent and we strongly recommend it to ophthalmologists working in India.

E. O'G. K.

**AN INTRODUCTION TO CLINICAL PERIMETRY.**—By H. M. Traquair, M.D., F.R.C.S. (Edin.). Fourth Edition. 1942. Henry Kimpton, London. Pp. xv plus 332. Illustrated (245 illustrations and 3 coloured plates). Price, 30s.

THIS well-known book first published in 1927 deals with the methods of visual-field testing in which the author describes, and explains a simple procedure which the experience of others as well as himself has shown to be both easy and satisfactory. This procedure is that known as the quantitative method of perimetry

which is essentially the method of Bjerrum, who discovered nearly fifty years ago that he could obtain more information by using the back of his consulting room door than he could from the ordinary perimeter.

The contents are divided into two parts. Part one has an introduction and chapters on the normal field of vision, perimetric instruments, methods of examination and the physiology of the visual field in relation to clinical perimetry. Part two deals with applied perimetry the function of which is to discover the cause of depression of vision not adequately explained by other methods of examination and also to measure the degree and progress of the morbid process. It consists of an introduction and chapters on the pathological field, the interpretation of changes in the visual fields, the choroid and retina, glaucoma, the optic nerve, the chiasma, the supra-chiasmal pathway and functional changes in the field of vision. There is also an appendix with articles on isopters for white and colour in the normal field, the blind spot, the anatomical relations of the visual pathway, the sheath and connective tissue framework of the optic nerve, the blood supply of the visual nerve path, the uses of the perimeter and screen otherwise than in field testing and tables of tangents and degrees for use with Bjerrum's screen.

As in the third edition, there is a foreword by Mr. Dott who points out forcibly the value of perimetry from the standpoint of the neurologist and the neurosurgeon.

The fourth edition of this excellent book has not undergone much alteration; two figures have been altered, eighteen new figures, forty-five new references have been added and several passages have been simplified.

The whole medical profession owes a great debt to Dr. Traquair for his work on perimetry and for placing at its disposal an eminently practical guide to the technique of visual-field testing.

We strongly recommend this book to ophthalmologists as a classic of its kind, and consider a copy of it is essential. It should be in the possession of every medical man interested in eye work in India.

E. O'G. K.

**THE PRACTICE OF REFRACTION.**—By Sir Stewart Duke-Elder, M.A., D.Sc. (St. And.), Ph.D. (Lond.), M.D., Ch.B., F.R.C.S. Fourth Edition. 1943. J. and A. Churchill Limited, London. Pp. xii plus 328, with 183 illustrations. Price, 15s.

THIS is the fourth edition of this book which alone speaks for its popularity. It consists of six sections, on eye strain, refraction, accommodation and convergence, muscle balance, clinical methods, spectacles, and six appendices.

The author presents the subject in a simple and essentially non-mathematical form wherein all that is necessary for the clinical practice of refraction is described. The book is therefore clinical rather than theoretical, and the object is essentially practical. The author very wisely points out that whatever the type of book the would-be refractionist uses, it cannot be insisted upon too strongly that the art of refraction cannot in any sense be learned by reading, and that the only way to obtain efficiency is by prolonged and painstaking practice in the extern department of an eye hospital in which large numbers of cases of all kinds are available and where the findings can be checked by experienced refractionists. In the new edition, owing to the exigencies of military service, few changes have been made, and so the book retains the essential character of its predecessor.

The book is excellent and we can only suggest that in the next edition the chapter on protective glasses be altered as there are better tinted glasses for use in the tropics than Crookes's glass to diminish the intensity of the luminous rays and at the same time to shut out excess of the ultra-violet and infra-red rays such as Polaroid and the various kinds of Ray Ban and Colobar. We strongly recommend the book to students

E.B. 6



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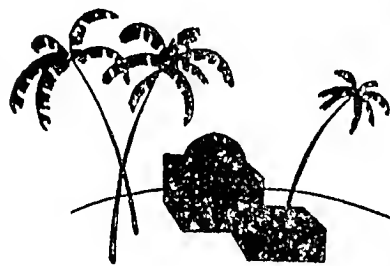
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## Abstracts from Reports

REPORT OF A MEETING OF THE ROSS INSTITUTE INDUSTRIAL ADVISORY COMMITTEE HELD IN THE COUNCIL CHAMBER OF THE RUBBER GROWERS' ASSOCIATION, 19, FENCHURCH STREET, LONDON, E.C. 3, ON THURSDAY, 27TH MAY, 1943, AT 2-30 P.M.

THE Ross Institute is a branch of the London School of Hygiene and Tropical Medicine and its Industrial Advisory Committee was formed in 1928 to make the tropics healthy for industry. At its fourteenth meeting held in London in last May the activities of the Institute in India, Ceylon and Africa were reviewed. Sir Malcolm Watson who has retired from the post of Director and is now Honorary Consultant referred to the biological methods of malaria control and predicted that in the immediate future there would be vast epidemics of malaria in many parts of the world as a result of the war. Dr. Wigglesworth and Prof. Leiper stressed the need for close collaboration between the field workers of the Institute and the scientific workers of the School. Col. Mackie dwelt on the problems of yellow fever in Africa and mentioned that the 'mouse protection test' showed that the disease was far more extensive than had been thought. Large numbers of the native population have been inoculated, he said, as a barrier against the transmission of the disease to India. Finally, reference was made to the malnutrition and disease among labour in East Africa due to inadequate food supply, and to make good, numbers of plantations are cultivating maize, millet and fruit trees. Although the chief aim of the Ross Institute is control of malaria, it now covers a far wider field in prevention.

DIRECTORY OF TUBERCULOSIS INSTITUTIONS IN BRITISH INDIA AND INDIAN STATES, 1943. PUBLISHED BY THE TUBERCULOSIS ASSOCIATION OF INDIA, 20, TALKATORA ROAD, NEW DELHI. Pp. 93. PRICE, AS. 12

THE Tuberculosis Association of India has just published a Directory of Tuberculosis Institutions in British India and Indian States. It contains a brief account of various tuberculosis institutions with special reference to their situation, climate, number of bed, types of accommodation, activities, medical staff, etc. Thus a ready and reliable information is available regarding facilities for the treatment of tuberculous patients at dispensaries, sanatoria and other institutions in different provinces and states. The book begins with a map showing special tuberculosis institutions in India up to 1943 and ends with an index of places where they are located. The price is annas twelve only, and copies can be had of the Secretary of the Association, 20, Talkatora Road, New Delhi.

## Correspondence

INTESTINAL TUBERCULOSIS: ITS DIAGNOSIS AND SIGNIFICANCE IN THE TREATMENT OF PULMONARY TUBERCULOSIS

SIR,—I am very much interested to read Dr. Frimodt-Møller's article in your October issue. He has described a case (case 1, p. 516) of intestinal tuberculosis

in which he has observed hyperplasia with fold formation and numerous elevated areas, deep clefts and grooves in the caecum and ascending colon. It appears that this is a case of polypoid type of intestinal tuberculosis which we described (*Journ. Indian Med. Assoc.*, November 1941). As a matter of fact the picture of his case is almost an identical one with our case 7. This type is different from the usual ulcerative and frank tumour-like hyperplastic type.

B. P. TRIBEDI, M.B. (Cal.)  
D.B. (Lond.),

Professor of Pathology, Medical College, Calcutta, and Bacteriologist to the Government of Bengal.

CALCUTTA,

22nd November, 1943.

## Service Notes

### APPOINTMENTS AND TRANSFERS

MAJOR S. M. K. MALLICK assumed charge of the office of Principal, Medical College, Amritsar (previously Medical School), on the forenoon of the 6th October, 1943.

The services of Major C. K. Lakshmanan, Chief Health Officer, Delhi, are temporarily placed at the disposal of the Government of Bengal for appointment as Director of Public Health, Bengal, with effect from the 13th November, 1943, or the date on which he relinquishes charge of his present appointment.

Captain J. H. Caverhill, Staff Surgeon, Murree, relinquished additional charge of the Civil Surgeoncy, Murree, on the afternoon of the 18th October, 1943.

### INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

The undermentioned officer is transferred to the General Service Cadre, with effect from the date specified:—

Captain K. Krishnaswamy. Dated 18th June, 1943.

### To be Captains

Doraisami Sankaran. Dated 9th August, 1943.

Priya Gopal Bhattacharya. Dated 18th August, 1943.

Bindiganavale Krishnaiyengar Ramanna. Dated 12th September, 1943.

Krishna Chandra Mukherji. Dated 14th September, 1943.

Saradindu Mukerjee. Dated 13th October, 1943.

14th September, 1943

Suresh Chandra Dutta. Rash Behari Mukerjee. Prabhakar Dattatraya Bhawe. Dated 18th September, 1943.

Subimal Kumar Datta. Dated 15th September, 1943.

Ullal Maruthi Rao. Dated 4th October, 1943.

Susil Kumar Neogy. Dated 13th October, 1943.

14th October, 1943

Colin Henry Hope Robertson.

Mario De Menezes.

Homi Bomanji Parelwala.

Govind Vithal Joshi.

Amulya Ratan Roy.

Phanindra Nath Ray Chaudhuri.

Manchdivalakuth Mathew Alexander.

Bala Sphay. Jagdish Narain Mathur.  
Kuryan George. Dated 15th August, 1943.

15th October, 1943

Kamakhya Charan Ghosh.  
Kappagantu Venkatrama Sarma.  
Nirmal Kanti Nag. Dated 17th October, 1943.  
Binay Bhusan Bhattacharyya. Dated 19th October, 1943.

#### To be Lieutenants

Amar Nath Lokhotia. Dated 2nd April, 1943.  
Gurucharan Mookherjee. Dated 18th August, 1943.  
Cyvil Brondon Andrade. Dated 3rd October, 1943.

14th September, 1943

Behari Lal Verma. Dilip Kumar Roy Choudhury.  
Chandra Sekhar Prasad. Horisaday Chakravarty.  
Prafulla Kumar Chatterji. Sunilchandra Datta.  
Gobinda Pallab Ghosh. Sunil Kumar Sen.  
Amal Kumar Datta.  
Jagannath Chatterjee. Pratul Chandra Sinha  
Bhupaty Banerjee. Roy.  
Jitendra Chandra Chatterji. Praphulla Kumar Chakravarti.

15th September, 1943

Sadr-ul-Islam Mohammad Kazi Abul Monsur.  
Golam Mannan. Manik Ratan Sarkar.

17th September, 1943

Satya Pal Gulati. Kesur Singh Kochhar.  
Fahim Ahmad Khan. Charles Walker Bamford.  
Thomas Clement Hopkins-Hussan. Dated 27th November, 1942.  
Francis Walter Perreira. Dated 4th April, 1943.  
William Burbridge James. Dated 29th July, 1943.  
Shanti Kumar Mitra. Dated 14th August, 1943.  
Noel Vernon Doyle. Dated 30th September, 1943.  
Cecil Herbert Drake. Dated 18th August, 1943.  
Guy Terence Wallace. Dated 17th September, 1943.

14th October, 1943

Tandemati Venugopala Rao. Sisir Kumar Ray.  
Ajit Kumar Ray. Eric Joseph Newton.  
Arthur Rothschild Coshun. Dated 19th October, 1943.

The undermentioned officers of the I.M.S. (E.C.) revert from I.A.M.C. and are seconded for service with the Royal Indian Navy:—

#### INDIAN LAND FORCES

##### INDIAN MEDICAL SERVICE

##### (Emergency Commissions)

Captain B. Singh. Dated 1st October, 1943.  
Lieutenant J. N. Chatterjee. Dated 9th October, 1943.  
Captain G. P. Ramayya. Dated 21st October, 1943.

#### (WOMEN'S BRANCH)

##### To be Captain

(Miss) Sarah Abraham Shellim. Dated 25th September, 1943.

##### To be Lieutenants

(Miss) Sarah Isaac Jacob. Dated 12th October, 1943.  
(Miss) Shafiq Aziz. Dated 18th October, 1943.

#### PROMOTIONS

Lieutenant-Colonel A. H. Harty, C.M., Inspector-General of Civil Hospitals, C. P. and Berar, has been promoted to the rank of Colonel, with effect from 9th August, 1943.

##### Major to be Lieutenant-Colonel

K. S. Fitch. Dated 13th October, 1943.

##### Captain to be Major

G. P. Charlewood. Dated 17th June, 1943.

#### LAND FORCES

##### INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY MEDICAL CORPS

##### (Emergency Commissions)

##### Lieutenants to be Captains

G. Skinner. Dated 8th September, 1942.  
A. W. Howarth. Dated 10th January, 1943.  
P. R. W. Leigh. Dated 14th March, 1943.  
S. C. Macmillan. Dated 27th April, 1943.  
M. E. Tapissier. Dated 11th May, 1943.  
G. O. W. Millington. Dated 8th August, 1943.  
C. M. Rogan. Dated 8th August, 1943.

#### RETIREMENT

Lieutenant-Colonel P. A. Dargan. Dated 6th September, 1943.

#### RESIGNATIONS

##### INDIAN LAND FORCES

##### INDIAN MEDICAL SERVICE—SECONDED TO INDIAN ARMY MEDICAL CORPS

##### (Emergency Commissions)

The undermentioned officers are permitted to resign their commissions:—

Captain P. K. Basu. Dated 26th April, 1943.  
Lieutenant Phanindra Chandra Sen. Dated 7th October, 1943.

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## Original Articles

## THE TREATMENT OF KALA-AZAR WITH DIAMIDINO-DIPHENOXY-PENTANE (M&amp;B 800). FINAL RESULTS OF TREATMENT OF THE FIRST 32 CASES

By P. C. SEN GUPTA, M.B. (Cal.)

*Officer-in-charge, Kala-azar Research Department,  
School of Tropical Medicine, Calcutta*

EARLY last year, Napier and Sen Gupta (1943) published a preliminary report on the treatment of kala-azar with 4:4' diamidino-diphenoxy-pentane. Thirty-two cases of kala-azar, 11 of which were 'resistant' cases, were treated, and 10 out of these 11 cases and 19 out of the remaining 'ordinary' cases made a prompt recovery. Two patients died of associated complications during the course of treatment and in one patient the drug was unsuccessful in effecting a clinical cure. The dosage scheme of the drug was not different from that followed in the treatment of kala-azar with diamidino-stilbene (Napier, Sen Gupta and Sen, 1942).

From the all-round clinical improvement of the cases that showed clinical cure, it was felt probable that all these cases had made a complete recovery, but the writers pointed out that clinical criteria of cure as well as the protozoological might be quite misleading, and that time only could show whether the clinical cure indicated a complete recovery or not. It was not possible at the time to present a follow-up report of these cases, as in most of them the treatment had finished less than four months before the publication of the preliminary observations.

In the present paper it is proposed to set forth the results of follow-up of these cases who showed clinical recovery, for a period of not less than 6 months after the completion of treatment.

The patients who were either seen to be in good health or who replied saying that they were in good health, free from fever and enlargement of the spleen have been classed as 'cured'. All cases that relapsed came under observation and were treated subsequently with antimonials or diamidines. The second case (Case 29), in which the treatment was unsuccessful, required a course of neostibosan before she improved any further (*i.e.* in Hb. %, R.B.C. and W.B.C. count, size of spleen, etc.) than was reported in the previous communication. A number of patients could not be traced; this was probably due to change of address caused by war conditions.

From the table it will be seen that there was a relapse in no less than 12 cases, *i.e.*

TABLE\*

Result	Case numbers	Total
Cured ..	3, 5, 13, 10(R), 14(R), 15(R), 17, 22, 23(R), 25.	= 10 cases
Relapsed ..	1, 2, 4, 8, 9, 12(R), 16, 18, 20(R), 30, 31(R), 32(R).	= 12 "
Untraced ..	7, 19, 21(R), 26, 27, 28	= 6 "
Failures ..	24, 29(R)	= 2 "
Died during treatment.	6(R), 11	= 2 "
	TOTAL ..	= 32 cases

\*The case numbers are the same as in protocol I of the paper on preliminary observations (Napier and Sen Gupta, *loc. cit.*). (R) signifies a 'resistant' case.

in over one-third of the total cases and over one-half of the treated cases. This is much higher than is seen with the pentavalent antimonials and diamidino-stilbene.

There is apparently no relation between the occurrence of relapse and the type of the case, *viz.* ordinary or 'resistant'. About half of each group of cases which could be traced showed relapse. The dosage employed does not seem to be responsible. In the group of cases which relapsed, the mean total dose per 100 lb. body-weight was  $0.969 \pm 0.4305$  gm. and the dose in the cases who made a complete recovery was  $1.025 \pm 0.1793$  gm. The difference between these two is not significant.

## Conclusion

From the above consideration of the final results of treatment of kala-azar with diamidino-diphenoxy-pentane (M&B 800), with a dosage scheme similar to that used for diamidino-stilbene, the following conclusions appear justified :—

The drug undoubtedly possesses some degree of curative action in Indian kala-azar, because in a high proportion of both ordinary and 'resistant' cases a prompt clinical cure can be achieved. But the drug may completely fail in a few cases (2 out of 32 cases).

Moreover there is a relapse of kala-azar within 6 months in more than one-third of the cases (12 out of 30 cases) showing prompt recovery. This relapse rate is much higher than that seen in cases treated with diamidino-stilbene. With diamidino-stilbene not more than 5 out of 104 cases are known to have relapsed.

Because of the high relapse rate the drug is inferior to diamidino-stilbene and to the best pentavalent antimonials as a curative agent in Indian kala-azar.

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- NAPIER, L. E., and SEN GUPTA, P. C. (1943). *Indian Med. Gaz.*, **78**, 177.  
NAPIER, L. E., SEN GUPTA, P. C., and SEN, G. N. (1942). *Ibid.*, **77**, 321.

## THE TREATMENT OF KALA-AZAR COMPLICATED WITH PULMONARY TUBERCULOSIS

By P. C. SEN GUPTA, M.B. (Cal.)

Officer-in-charge, Kala-azar Research Department,  
School of Tropical Medicine, Calcutta

THE difficulty of treatment of kala-azar when associated with pulmonary tuberculosis has been recognized by all workers who have come across such cases. Napier (1937) considered pulmonary tuberculosis and kala-azar to be a fatal combination. He had observed that when kala-azar and pulmonary tuberculosis co-existed, antimony treatment had little or no effect on the symptoms, fever and splenic enlargement, and that, on the other hand, the lung lesions underwent rapid extension when antimony was given. The antimonials were the only specific for kala-azar, and these had a malign influence on the course of pulmonary tuberculosis. Napier (*loc. cit.*) considered that there seemed to be a possibility that by using a small dosage in these cases, one might cure kala-azar without producing the unfavourable reaction. In any case, he felt that this was the only course to follow, because it was but rarely that kala-azar underwent spontaneous cure, and it was unlikely that one could stop the tuberculous process in a patient in whom the leishmanial infection was active.

But there is a definite relationship between the total dosage of antimony compounds and the cure rate. There is a certain dosage which gives the highest cure rate. With a dosage smaller than this, the chances of relapse are greater, and relapsed cases with pulmonary

diamidines tested so far, diamidino-stilbene is by far the best, and that, while having certain disadvantages, it has a curative action equal to the best pentavalent antimony compounds.

The writer, who earlier this year treated a case of kala-azar, complicated with what proved to be a pneumonitis, with diamidino-diphenoxypentane (pentamidine, M&B 800) without causing an exacerbation of the lung symptoms, felt that it might be possible to treat the leishmanial infection in a case complicated with pulmonary tuberculosis by means of the aromatic diamidines without causing a 'flare up' of the lung lesion.

The following case-report will illustrate the effect of treatment of kala-azar with diamidino-stilbene in a young adult showing bilateral tuberculous disease of the lungs.

### Case note

M. I., an Indian male, aged 18 years, was admitted into the hospital of the Calcutta School of Tropical Medicine on 22nd July, 1943, for fever, duration 3 months, cough with slight expectoration—1 month. The patient gave a history of having hæmoptysis on two occasions, once two years ago and again 1½ years ago.

On admission the patient was found to be weak and anæmic, and there was œdema around the ankles. The weight was 76 lb. Pulse/respiration = 126/28 per minute, temperature—101°F. The lungs showed impairment of percussion note and crepitations over the right apex, subclavicular and suprascapular regions. There were a few scattered rhonchi over the left side. Heart—no abnormality; liver—enlarged to 2 inches below costal margin; spleen—enlarged to 6 inches below the tip of the 9th left costal cartilage.

The aldehyde test and the complement-fixation test for kala-azar were positive. Sternal puncture showed Leishman-Donovan bodies. No acid-fast bacilli were present in smears made from the sputum. For blood count, see table.

### Blood counts

Date	Hb. in gm. %	R.B.C. in millions per c.mm.	Mean corpuscular volume (cu. $\mu$ ).	Mean corpuscular hæmoglobin ( $\gamma\gamma$ ).	Mean corpuscular hæmoglobin conc. (%)	W.B.C. in thousands per c.mm.	Neutrophil %	Lymphocyte %	Monocyte %	Eosinophil %	Van den Bergh test
27-7-43	5.5	2.47	82.9	22.3	26.8	2.1	55	25	15	5	Neg.
24-9-43	12.375	4.98	80.32	24.8	30.9	11.4	55	27	5	13	"

tuberculosis present far greater difficulties in treatment. Thus lowering the dose of the antimonials is perhaps not likely to provide a solution to the problem.

The introduction of the aromatic diamidines in recent years has provided us with a group of compounds having a specific curative action in kala-azar. The work during the last three years on Indian kala-azar (Napier, Sen Gupta and Sen, 1942; Napier and Sen Gupta, 1943; Sen Gupta, 1944) has shown that, of the aromatic

The patient was treated as a strict bed case and he was put on a course of injections of diamidino-stilbene (M&B 744). The injections were given intravenously on alternate days. Ten injections were given from the 27th July, 1943 to 14th August, 1943; the total dose was 0.675 gm. and the relative total dose per 100 lb. body-weight was 0.89 gm. In addition to the specific treatment, the patient had symptomatic treatment to relieve his irritant cough. The temperature started coming down after the



Fig. 2.—Skiagram of chest taken before commencement of treatment. (20-7-43.)



Fig. 3.—Skiagram of chest taken after treatment. (23-9-43.)

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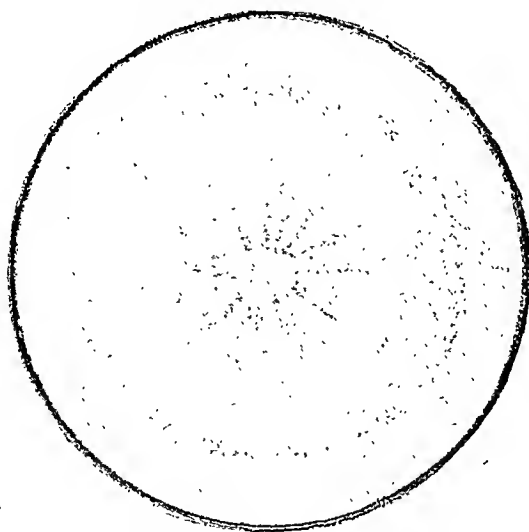


Fig. 4.—Showing the characteristic growth in culture.





Fig. 1a.



Fig. 1b.

Showing the characteristic patches.



Fig. 2.—Microsporon infection of the neck.

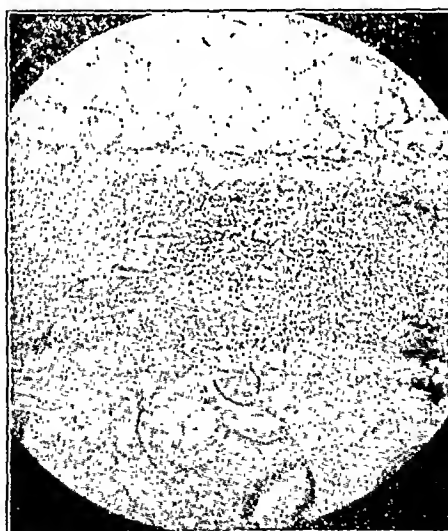


Fig. 3.—Caustic potash preparation of the hair showing the mosaic pattern of the spores.

second injection, and it remained normal from the day after the completion of the course of injections (see figure 1). The patient was put on a liberal diet as soon as the temperature showed a tendency to come down to normal. He was given cod-liver oil and calcium salts by mouth. About a fortnight after the course of M&B 744, the patient was put on cinchona febrifuge gr. x b.d. for 7 days, to eradicate any latent malarial infection. The splenic enlargement gradually came down and on 13th September, 1943, the tip of the spleen was only 2 inches below the 9th costal cartilage; the patient had gained 8 lb. in weight, and was almost free from cough. He was then put on a course of ferrous sulphate as there was a slight degree of hypochromia present.

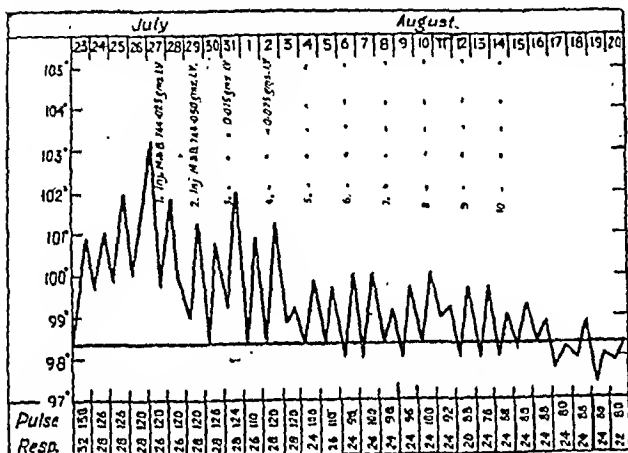


Fig. 1.

The patient was discharged from the hospital on the 24th September, 1943, with advice to attend a chest diseases clinic. He was quite free from fever, the pulse and respiration rates were normal. The spleen was soft and replaceable under the costal margin. The weight was 88½ lb. indicating a gain of 12½ lb. The blood count was within the normal range for Indians as far as Hb. and RBC were concerned, and there was a slight degree of leucocytosis. A skiagram taken on the 23rd September, 1943, showed that there was no exacerbation of the pulmonary lesion, and the lesion on the right side showed more fibrosis.

Report on the skiagrams (figures 2 and 3, plate I) taken before and after treatment, by Dr. P. K. Sen.

*Before* (20th July, 1943): The skiagram shows intermediate type of infiltration (exudative and reparative processes are present in almost the same degree) with cavitations in the upper and middle zones of the right lung. Upper and mid zones of the left lung are also involved. The lesions are mostly fibrotic. A cavity is present in the upper zone.

*After* (23rd September, 1943): The lesions in the right lung show more fibrosis. There is no extension of the disease. The lesions in the left lung are almost in the same condition as before.

It will be seen from the notes of the case that the treatment of kala-azar with diamidino-

(Concluded at foot of next column)

## STUDIES OF RINGWORM

## PART I

## MICROSPORUM AUDOUINI INFECTION IN INDIA

By N. C. DEY, M.B., B.Sc.

and

L. M. GHOSH, M.B., D.T.M.

From the Medical Mycology Enquiry, School of Tropical Medicine, Calcutta (financed by the Indian Research Fund Association)

*Introduction.*—Microsporosis, or infection by the small-spored ringworm fungus, was first described by Gruby in 1843, and the fungus which infected the hair of a child was named *Microsporum* (*Microsporon*) *audouini* by him. Gruby also gave a good description of the fungus. After Gruby, very little work was done till

(Continued from previous column)

stilbene did not cause any exacerbation of pulmonary tuberculosis. The fever came down and the splenic enlargement subsided almost completely, and there was a marked improvement in the blood count. As diamidino-stilbene was used in a dosage adequate to cure an untreated case, the patient has a 95 per cent chance of being permanently cured of kala-azar. General symptoms and radiological evidence pointed to the fact that the pulmonary condition was not aggravated in any way but, on the other hand, had improved to some extent, and with the general health much improved, it is likely that the patient will more readily respond to therapeutic measures against pulmonary tuberculosis.

Though it is not justifiable to come to a definite conclusion regarding the treatment of any condition on the experience of a single case, the striking success that has attended the treatment of visceral leishmaniasis in this patient, who had pulmonary tuberculosis as well, leads the writer to hope that probably in diamidino-stilbene we have a highly specific anti-kala-azar drug which, unlike the antimonials, will not cause an exacerbation of pulmonary tuberculosis, and it may be possible now to treat what Napier called a fatal combination with more hope of success. However, this hope can only be fully justified when similar success is obtained in a large number of cases by different workers.

## Acknowledgment

The writer is thankful to Dr. P. K. Sen, M.B. (Cal.), M.D. (Berlin), Ph.D., T.D.D. (Wales), of the chest department, Calcutta Medical College Hospitals, for the report on the skiagrams.

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- NAPIER, L. E. (1937) .. *Indian Med. Gaz.*, **72**, 242.  
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 SEN GUPTA, P. C. (1944). *Ibid.*, **79**, 49.

1892, when Sabouraud proved that the fungus described by Gruby was the cause of the common ringworm of the scalp in children. Later Sabouraud and Bodin described some more species in the genus *Microsporum*. Similar investigations in England by Adamson (1895) and Fox and Blaxall (1896) confirmed Sabouraud's work. These authors were also able to differentiate the two main groups in the genus *Microsporum*, namely, the human type, transmitted from one human being to another, and the animal type of which the source of infection is usually a pet, e.g. cat, dog, horse, etc. Inflammatory conditions and suppuration are more common in the animal type of microsporiasis than in the human type.

**Epidemiology.**—It is a highly contagious disease amongst children—the contagion spreading from one child to another through infected hats, towels, hair-brushes, combs, etc. The disease is found mostly in orphanages and in boarding schools. From the school the children bring the infection to their homes and give it to their brothers and sisters, who in turn spread the disease amongst their playmates in the neighbourhood.

The human type of microsporum is more frequently met with than the animal type, and *Microsporum audouini* is the most common species in this group. In England, 90 per cent of the hair ringworm in the children is due to *Microsporum audouini*; in France (Paris) 60 per cent. It is not so common in Germany, Sweden and in eastern Europe. In India the incidence of microsporiasis has not been recorded in the literature available here. Its occurrence was first mentioned by Dey and Maplestone (1935). Out of 182 consecutive cases of ringworm of the scalp in which the causative organisms were determined, 85 cases were due to microsporum infection, and of these 85 cases, 77 or 94.1 per cent were due to *Microsporum audouini*, and 8 cases were due to *Microsporum ferrugineum*. These 8 cases of *M. ferrugineum* were reported by Maplestone and Dey (1939). The majority of these cases came to Calcutta for treatment from the different hill station schools in India; only a few were from the local schools, where the infection could not be definitely traced to the hills. All these 85 children were of non-Indian origin.

**Ætiology: Age.**—Ringworm of the scalp is essentially a disease of the children; this is especially so with microsporum infection.

Children of the school-going age, that is from five to fifteen years of age, are the worst sufferers. Microsporiasis undergoes spontaneous cure as the patients attain puberty, and its occurrence after puberty is extremely rare. Macleod recorded only 2 cases, and in both cases the mother got the infection from her children.

Both sexes are equally affected.

A characteristic feature of the incidence of microsporum infection in India is that so far no case has been reported amongst Indian

children in the plains. In all the instances that we have seen, the patients were non-Indian—European, Anglo-Indian, Jew, etc. This fact was reported by Ghosh (1941).

**Description and progress.**—The initial lesion is one or two small white scaly patches in which the hairs appear to have thinned out or to be entirely absent. When carefully examined, the patches are found not exactly bald, but the surface is covered with thin white scales, and the hairs are broken, leaving small stumps about  $\frac{1}{4}$  inch long sticking out in different directions from underneath the scales. Owing to these white scales on the patches, the condition is called 'scaly ringworm' (figure 1, a and b, plate II).

The patches are usually of 1 inch to 2 inches in diameter, sometimes larger, when first noticed; they extend by contiguity and continuity, become larger, and at the same time other fresh areas may be affected. In trichophytosis the patches are usually small, but multiple patches appear from the start and very soon the whole scalp appears to be riddled with small patchy bald areas.

The infected hairs are thin, lustreless and brittle. They break off, leaving stumps of about  $\frac{1}{4}$  inch or  $\frac{1}{8}$  inch long pointing in different directions. The infected hairs are loose, and can be easily pulled out by a gentle steady pull with a pair of epilation forceps. The infection first starts on the surface of the scalp where it causes a mild inflammation and slight desquamation. The mycelial threads then pass downwards in the hair follicle along the side of the hair near its root. Near the bulb the fungus penetrates the cuticle, gets inside and spreads upwards along the shaft to about  $\frac{1}{4}$  inch above the surface of the scalp. This portion of the hair, from near the root to  $\frac{1}{4}$  inch above the surface of the scalp, is enveloped in a white sheath formed by the spores of the fungus arranged in a mosaic pattern.

**Course.**—If left untreated, the patches grow larger, and fresh patches appear in other places. The older patches become bald, due to the loss of the hairs from the root, and this baldness is permanent. In patients nearing puberty, spontaneous cure is seen.

From the hairy scalp the infection may extend to the glabrous skin on the face or forehead, and to the neck (see figure 2, plate II) near the margin of the scalp as a direct spread from the hairs. The lesions on the skin are usually small scaly patches with irritation.

As mentioned before, the majority of the cases come from the hill stations, but the progress of the disease is not affected or altered when these children come down to the plains.

**Symptoms.**—In early cases there is scarcely any subjective symptom besides slight irritation and consequent scratching of the head, which often goes unnoticed. The first case is usually detected when the disease is fairly advanced, and then the other cases are found by careful

examination of the contacts. Sometimes the ringworm is first suspected when the child complains of pain and irritation due to inflammation from secondary infection consequent to scratching, or when the child is seen to scratch the scalp constantly. *Microsporum audouini* rarely causes a primary inflammatory condition as do some of the animal microspora.

**Diagnosis.**—It should always be borne in mind that ringworm of the scalp is essentially a disease of the children. The presence of one or more bald patches on the scalp of a school-going child with or without the stumps of the broken hairs almost certainly indicates ringworm infection. The white scaly surface of the scalp in the patches, together with small stumps of the broken hairs sticking out in different directions from underneath the scales, and the absence of multiple small lesions are characteristic of a microsporum infection. The absence of inflammation points towards its being a microsporum of human type.

If a few of the suspected hairs are pulled out and placed on a glass slide, and a drop of chloroform is put on them, the infected hairs look chalky white. In all doubtful cases, microscopic examination of the suspected hairs should be resorted to.

In cases of *Microsporum audouini* infection Wood's light is of great value as an aid to diagnosis and also to the assessment of the progress and cure. Wood's light is an arrangement whereby ultra-violet rays from a mercury vapour lamp are passed through a piece of dark purple glass containing nickel oxide. This glass plate acts as a light filter allowing ultra-violet rays of longer wave-lengths than 3,000 A.U. to pass through it. The rays passing through this filter give a peculiar greenish fluorescence to the infected hairs; this fluorescence is very characteristic. The subjects are examined in a dark room with the scalp cleaned with ether and alcohol to remove any grease. The affected area or areas are easily detected by the green fluorescence from the infected hairs. Wood's light is of great help in the examination of the contacts and in detecting early cases when the patch is a small one and easily missed. It is also of great value in determining the progress of cases while under treatment. Before declaring a case cured, examination by Wood's filter should be resorted to, but it should be remembered that the usefulness of the Wood's light is limited to microsporum infection only.

**Prophylaxis.**—Ringworm of the scalp is a highly contagious disease of common occurrence amongst school-going children, especially in boarding schools. From the school the child carries home the infection and spreads it to his or her brothers and sisters and the playmates in the neighbourhood. Every possible care should be taken to have the children's scalp thoroughly examined before admission to a school, and periodical examination every two or three months

should be done and careful search should be made to detect the infection.

As soon as the infection is detected, the child should be sent away for treatment, and classmates, room-mates and other associates should be segregated and thoroughly examined every week for four weeks. Every possible care should be taken to detect the early infection, and Wood's filter is particularly valuable for this purpose. The hats, hair-brushes and combs of all the contacts should be thoroughly sterilized or, where this is not possible, destroyed.

**Treatment.**—As soon as the diagnosis is established, the hair of the whole scalp should be cut short, and clipped close to the surface. This is essential and must be insisted on; otherwise some early patches may escape detection and treatment. The hats, hair-brushes, etc., must be destroyed and the child given tight-fitting linen caps to wear continuously during the whole period of the treatment. These caps are changed every morning or twice daily, and boiled thoroughly before further use. The use of the caps prevents the infected hairs being scattered about.

The actual treatment consists of quickly removing the infected hairs by the root, and the use of a fungicide to kill the fungus infecting the surface of the scalp. Any good fungicidal remedy is strong enough to kill the organism if it can be brought into contact with the fungus. Microsporum infection being mainly in the hair root and in the parts of the hair which remain inside the hair follicle, fungicidal remedies by themselves are of no use. The first step is to remove the infected hair—a task which is not easily performed.

Hairs may be removed by any of the following methods :—

(1) Manual epilation.—The infected hairs are pulled out as quickly as possible with a pair of epilation forceps. This process is very unsatisfactory and tedious, and requires a good deal of training and skill.

(2) Local application of irritant drugs.—To produce acute inflammation in the affected areas, so that the hair follicles dilate and the hairs become loose and are easily pulled out. The drugs usually employed are :—

(a) Croton oil applied pure or in 5 to 10 per cent ointment. This is rubbed in once or twice daily followed by a warm boric fomentation. This is continued till an acute inflammatory condition is produced and the diseased hairs become loose and are easily pulled out. The oil is then replaced by a soothing fomentation or application. This method is very painful and may prevent sleep. Children under five years of age should not be given this treatment.

(b) Ordinary sodium chloride made up into ointment with equal parts of vaseline when rubbed over the patches for a few minutes twice every day produces acute inflammation so as to cause epilation easy.

(c) Chrysarobin in the form of an ointment 2 per cent to 6 per cent with lanoline, or a paint with acetone or collodion applied over the patches also produces the same effect. But the application of chrysarobin should be avoided on any part above the neck, as it may get into the eyes and cause severe conjunctivitis. Moreover the method is also very painful.

(3) Thallium acetate internally.—Thallium acetate when given internally in proper doses (8 milligrammes per kilogramme of body-weight, given in one single dose) loosens the hair roots and all the hairs come out easily when pulled. But thallium acetate is a toxic drug, and the therapeutic and toxic doses are so near to each other that its administration is risky. A detailed description of the method of administration of the drug is given in all the standard books on dermatology, and is not repeated here.

(4) Depilation by x-rays.—This is an easy and satisfactory method of depilation in skilled and expert hands; otherwise this is also fraught with grave danger. Burns or permanent baldness may result.

The routine treatment that is carried at the Calcutta School of Tropical Medicine is as follows :—

(a) The hair of the whole scalp is clipped short, and tight fitting linen caps are worn. The hair is clipped every week till the child is declared cured.

(b) All the affected patches are detected; the help of the Wood's light is taken if necessary.

(c) The mother or the nurse of the child is taught to detect and pull out the infected hairs with a pair of epilation forceps. This they have to do for two hours every day, picking out as many diseased hairs as possible. (It is important that these hairs are placed in an envelope and burnt every day.)

(d) After the two hours' sitting every day, the scalp is shampooed well with a spirit soap lotion containing soft soap 1 ounce and rectified spirit 2 ounces.

(e) After the shampoo, one of the lotions or ointments mentioned below is rubbed in.

(f) The child is examined once every week after the shampoo but before any medicine is applied, and further instructions are given to the parents.

(g) If the child is not cured by this treatment, then depilation by x-ray is advised.

About half the cases have responded well to this conservative treatment, and have been cured. It is true that this treatment takes a very long time and is tedious and troublesome, and that the results are uncertain, but the risks attending the other two methods are avoided.

X-ray treatment is given under the following conditions :—

(a) If the infection is very advanced, affecting large areas of the scalp, and if chances of recovery by other methods are remote.

(b) If there are already many bald patches due to the scars.

(c) If the infection is from an animal parasite spreading rapidly and causing an inflammatory condition and secondary infection.

(d) If the subject is a boy and the parents want a quick cure.

(e) When the other methods have failed to cure the condition and the parents are willing to take the risk of the x-ray treatment.

About three weeks after the application of the x-rays, the hairs begin to fall off. A mild antiseptic soothing lotion is used during this intervening period, and, once the hairs come off, no further treatment will be required but the same lotion may be continued. The lotion that is usually given consists of resorcinol—dr.  $\frac{1}{2}$ , perchloride of mercury—gr.  $\frac{1}{2}$ , rectified spirit—dr. 1, tincture of lavender—dr. 1, water to 1 oz.

When all the hairs have come off, the child may be declared cured and given new hats, hair-brush, etc., and allowed to go to school.

The ointments and lotions used for the routine treatment are :—

(1) Thymol	..	..	gr. v.
Oil cinnamon	..	..	℥ v
Liquor iodine	..	..	oz. i
To this may be added			
Acid acetic glacial	..	..	℥ x

(2) Liquor ferri perchloride.

(3) Merfenil gr. i dissolved in 5 c.c. of warm glycerine is mixed up well with two ounces of Whitfield's ointment.

(4) Phenol and camphor lotion.

Camphor	..	..	3 grammes.
Phenol	..	..	3 c.c.
when mixed will form a liquid to be applied.			

*Mycology.*—Examination of the hair.—Several suspected hairs are carefully pulled out by the roots with a gentle pull and are placed between two sterile glass slides and kept as stock. One or two hairs are then taken from the stock, and a coverslip preparation is made with a 40 per cent liquor potassæ solution and examined with  $\frac{1}{4}$ th objective. (A saturated solution of sodium sulphide with equal parts of alcohol is quicker in action but the solution does not keep long and should be prepared fresh.) The infected hair is seen to be covered with a sheath which is formed by clusters of small spores arranged in a mosaic pattern (see figure 3, plate II). This mosaic pattern is characteristic of the genus *Microsporum*. The spores are small in size, about  $3\mu$  in diameter, and may be round, oval or polygonal in shape. The spores are formed by fragmentation of the mycelial hyphæ. When the hair is cleaned and the spore sheath is removed from the surface, fungus mycelia with dichotomous branching may be seen in the medulla of the hair extending from the root.

*Culture.*—The hairs from the root should be cut into very small pieces in a sterile watch-glass and put up in the Sabouraud's medium, or in this medium with gentian violet (0.25 c.c. of 1/1000 solution of gentian violet in 100 c.cm. of Sabouraud's medium).

The primary culture usually appears on the third or fourth day after inoculation as fine silky fibres radiating from an inoculated piece of hair in an 'asterisk' manner, and the roots penetrate deep into the medium.

In the subculture the growth is usually round and shows radiating furrows from the central depression, and short white down on the surface (see figure 4, plate I). Subcultures on different laboratory media maintain the same character, and microsporon cultures do not readily undergo pleomorphic changes.

**Morphology.**—Our observations on the growth and morphology were made in welled-slide preparations and were as follows (see figure 5) :—

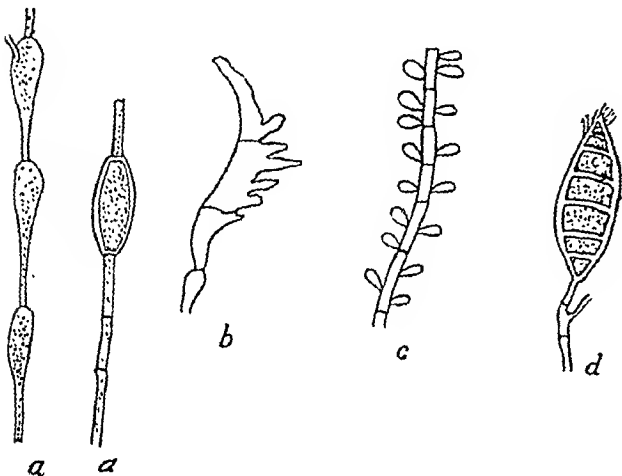


Fig. 5.—Showing (a) mycelial rackets; (b) 'pectinate' hyphae; (c) aleuriospores; and (d) spindles or 'fusseux'.

The mycelial filaments are usually fine, and the branching dichotomous.

(a) Mycelial 'rackets'.—While in the process of growth, the individual cells of certain mycelial hyphae are swollen at the distal ends and the hyphae give the appearance of a chain of tennis rackets. This appearance is said to be characteristic of the genus *Microsporum*. Some of the 'rackets' become chlamydospores by the formation of a double wall which cuts them off from the other cells of the same hyphae.

(b) 'Pectinate' hyphae.—These are comb-like projections from the ends of the hyphae limiting its growth. In *Microsporum audouinii* these are not so well developed as in *Microsporum lanosum*.

(c) Aleuriospores.—These are small lateral spores, oval or oblong and sessile, about  $3\mu$  to  $4\mu$  in length.

(d) Spindles ('fusseux' of the French authors).—These end-organs are spindle-shaped, being swollen at the middle and pointed at both ends. These may be septate or non-septate. They usually measure from  $30\mu$  to  $60\mu$  in length and  $15\mu$  to  $20\mu$  in breadth. Fine hair-like projections may be seen at the free end of the fusseux.

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## BASAL TUBERCULOSIS AND SELECTIVE PNEUMOTHORAX

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THE particular subject of basal tuberculosis in adults has attracted the attention of various authors. These forms were known long before the era of x-ray examination, although considered as extremely rare [Lacnec, 1831 (Hamilton and Fredd, 1935), Kidd (1886), Fowler, 1888 (Busby, 1939)]. More recent investigations of the last two decades brought forward many interesting details about the incidence, development, symptoms, treatment, etc., of basal tuberculosis, a short survey of which is given by Busby, 1939. The figures of incidence given by different authors vary between extreme rarity and 10 per cent; there is greater incidence in men than in women; the right lung is more often affected than the left. The character of the disease is said to be an acute exudative tendency not unlike tuberculous pneumonia or broncho-pneumonia. Signs and symptoms show great variety just as in any other form of lung tuberculosis.

Some confusion exists with respect to the topographical features of basal affections, because frequently the base is erroneously identified with the lower lobe, which actually forms only part of it. Topographically, the base of the lung is the lung surface in contact with the diaphragm. Clinically and radiologically, we understand by the term 'base' the lower third of the pulmonary area. The word 'base' is widely used in this sense, but like its fellow, 'apex', it is inaccurate but irreplaceable.

The base is divided into two very unequal parts by the greater fissure. Without considering anomalies of multilobed lungs, the base contains parts of at least two lobes. These are, on the right side, the funnel-shaped middle lobe, reaching the diaphragm by a narrow anterior zone only, and the lower lobe which forms the greater posterior part of the base. On the left side, the upper lobe is in contact with the lower lobe all along the fissure and thus descends deeply into the anterior part of the base. Basal tuberculosis, therefore, is not necessarily confined to the lower lobe; it may affect the middle lobe as well, or both. We shall see later that the lobar localization of a lesion may become an important factor in lung collapse in artificial pneumothorax treatment.

(Continued from previous column)

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Among the rare occurrences of multilobed lungs, one anomaly may appear more frequently than is generally recognized, viz, the cardiac lobe. According to Mollard, the cardiac lobe had been found (by Schaffner) in 45.6 per cent of cases. This lobe may easily escape our attention due to the fact that the middle lobe at the right side, or part of the upper lobe at the left side, covers it completely from the frontal view. Many surprising aspects of basal lesions and of basal collapse in artificial pneumothorax treatment will be elucidated if we think of the possible presence of a supernumerary cardiac lobe (see case 1).

In ordinary x-ray examination, the greater part of the base is well visible. There are, however, some important regions hidden by the shadows of the heart and diaphragm, which however may be seen in oblique and lateral positions of the chest. Technical details need not be discussed here, as they are mostly well known and adequately dealt with elsewhere.

In spite of improved technique, basal tuberculosis is rarely detected, at least in adults. This rarity is the more remarkable, as the base is known to show important lesions at the stage of first infection, being rather the predisposed part for primary tubercular implantation. (It goes without saying that basal tuberculosis proper does not include basal complications secondary to other lung foci, e.g. bronchogenous basal aspiration.) Basal tuberculosis is not always entirely confined to the base. Just as in other forms of lung tuberculosis, the basal disease may spread out. In advanced cases it becomes difficult to recognize the basal onset of the disease, unless the history of the case tells of the basal predominance of the affection. Simultaneous incipient lesions of both bases seem to be extremely rare.

Before diagnosing basal tuberculosis, we should beware of some possible causes of error. A photo taken in the expiratory phase of respiration often shows an accentuation or intensification of the basal markings, especially in females. Again, basal tuberculosis may be confused with mediastinal pleurisy, with para-vertebral abscess in tuberculous spondylitis, with bronchiectasis, lung abscess, hydatid cyst, asbestosis and other rare diseases.

According to Mollard, basal tuberculosis may originate at two different sites of the base, followed by more or less individual types of evolution. He discriminates between *tuberculosis of the exterior base* and that of the *interior base*. Personally, I am strongly inclined to add a third variety of *infra-hilar localization*. Examples of exterior basal affection may be seen in cases 1 and 2; interior basal affection is visible in case 3; the infra-hilar variety is shown in cases 4, 5, 6 and 7. In advanced extensive lesions, it may be difficult to recognize one of these three varieties, yet the site of the main cavitation may give a clue to the location of the incipient focus.

The first group, characterized by affections of the exterior part of the base, has great resemblance to what is called early infiltration,

although, on the whole, its course appears to be more acute: A congestive patch, mostly at the posterior peripheral part of the base, extends rapidly and, at the time of x-ray examination, shows already more or less advanced cavitation. Sometimes the peri-focal infiltration is soon absorbed, but an isolated, solitary, 'punched-out' cavity persists and increases gradually. At other times, the disease takes the course of a lobar, caseous pneumonia with the formation of irregular cavities.

The second group, typified by lesions of the interior basal part, is less striking in its clinical and radiological appearance than the former one. The affected part corresponds to what we may call the cardio-diaphragmatic triangle. Its clinical course is predominantly chronic or sub-acute. Radiologically we may place it with fibro-caseous and nodular forms of tuberculosis. Cavitation may occur early or late, showing a predominance of the 'moth-eaten' or bronchiectatic type. I have found it often very difficult to locate anatomically this type of basal lesion. Lower and middle lobes seem to be equally affected. A supernumerary cardiac lobe, if present, is apparently always involved. Sometimes, as mentioned by Busby, the location becomes evident after the establishment of artificial pneumothorax which often causes a radiologically clearer distinction of the lobes.

The third group, the infra-hilar type, is characterized by its close connection with the root of the lung, radiologically always more or less fusing with the hilar shadow. This form resembles very much a childhood type of tuberculosis which has been variously labelled as epi-tuberculosis, hilar-lung tuberculosis, gangliopulmonary tuberculosis, etc. Perhaps it is identical with these forms, as we find other childhood (haematolymphatic) forms occurring more frequently in adults of this country than in adults of the white races. The dense, confluent infiltration suggests a pneumonic form of the disease, which is generally confirmed by the acute signs and symptoms of the clinical picture. The lesion generally involves more than half the base adjacent to the hilar region. Solitary or multiple cavitation sets in rather early, and is mostly situated near the lower pole of the hilum. The lower and middle lobes of the right side may be equally affected, whereas the involvement of the left upper lobe seems to be at least very doubtful.

Pierret and his collaborators (1938) emphasized another topographical aspect of pulmonary infiltrations. In modification of the earlier French notion of lobitis (Leon Bernard's 'lobite'), they stress the importance of certain pulmonary sectors or zones of independent broncho-vascular supply which they think to be responsible for certain triangular infiltrations and, therefore, call 'zonitis'. With respect to the base they describe five zones: (1) middle dorsal, (2) inferior dorsal, (3) middle ventral, (4) inferior ventral and (5) an accessory, infra-cardiac zone. The last zone corresponds exactly with our above-mentioned second type of interior basal tuberculosis. The subdivision of the other zones seems radiologically less convincing to



Fig. 1a. Case 1.

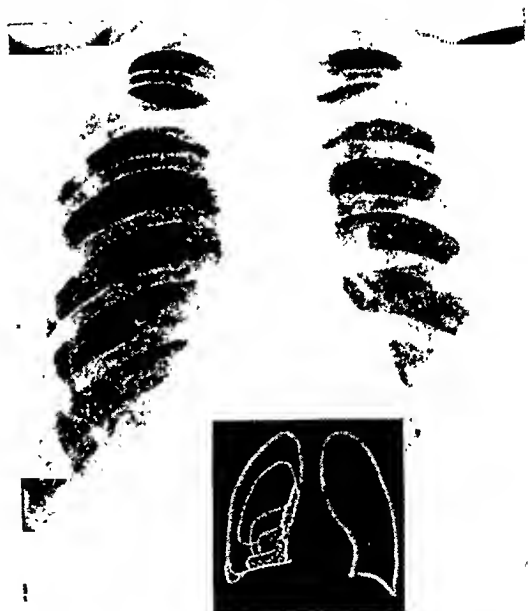


Fig. 1b. Case 1.

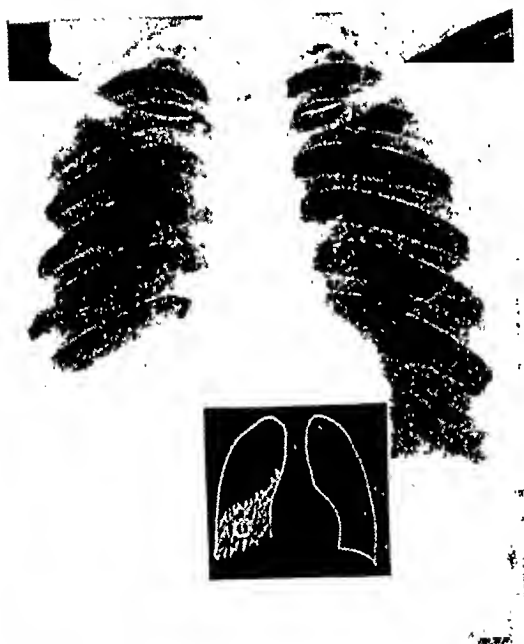


Fig. 2a. Case 2.

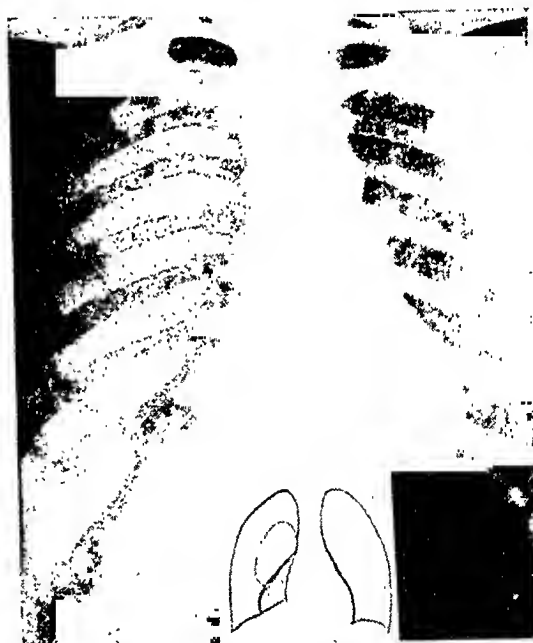


Fig. 2b. Case 2.

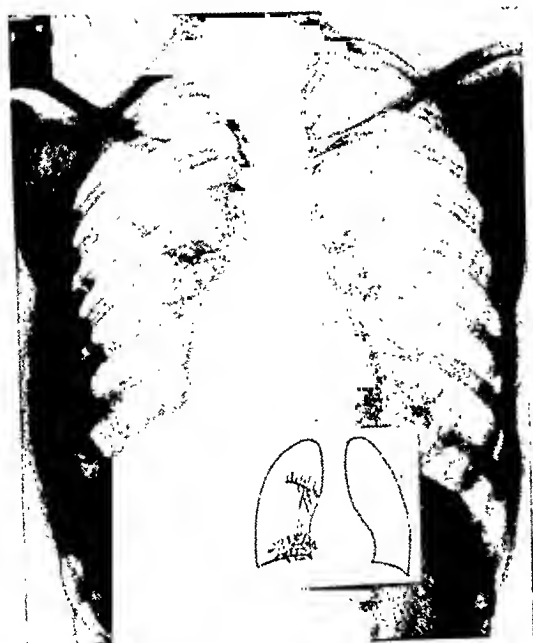


Fig. 3a. Case 3.

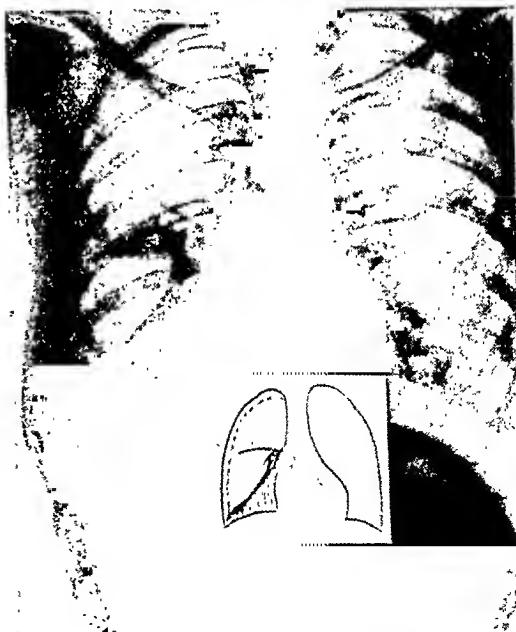


Fig. 3b. Case 3.

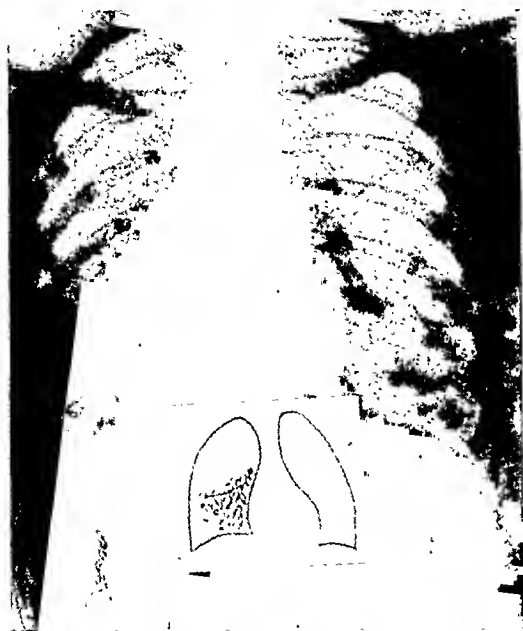


Fig. 4a. Case 4.



Fig. 4b. Case 4.



Fig. 5a. Case 5.



Fig. 5b. Case 5.

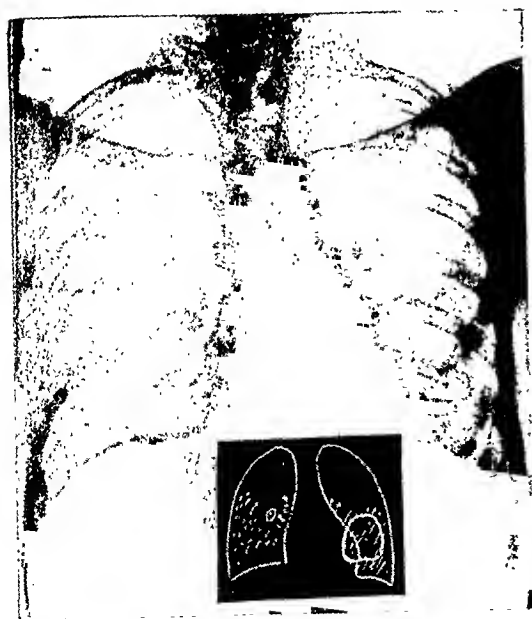


Fig. 6a. Case 7.



Fig. 6b. Case 7.

us, but the number of our observations is admittedly too small to justify a definite opinion.

With respect to therapeutical measures, Mollard attaches great importance to his differentiation into exterior and interior forms of basal tuberculosis. He believes that the former are suitable for collapse therapy, both artificial pneumothorax and phrenic interruption, whereas the latter should be treated on conservative lines. This therapeutical differentiation is not justifiable in our view. Without reference to any particular type of basal lesion, other favourable reports on collapse therapy are given by several authors. Gordon and Charr (1933) suggest that the combination of artificial pneumothorax and phrenic interruption is unusually effective for basal tuberculosis, a statement which we can fully support by one of our observations (case 2). Unfavourable reports are given by Widemann and Campbell (Busby, 1939) who are disappointed in the results regardless of the type of collapse therapy employed. Aguilar and Sirlin (1942) report that the lower lobe cavities gave the poorest result of all in responding to pneumothorax.

Only three reports have come to our knowledge mentioning a *selective collapse* in basal tuberculosis treated by artificial pneumothorax.

(1) Vaucher and Fath (Graham *et al.*, 1935), having observed one single case of selective artificial pneumothorax in basal tuberculosis, believe this to be a rare exception, and stress the point that only the upper lobe lesions are suitable for selective artificial pneumothorax treatment, whereas basal lesions almost preclude a selective collapse.

(2) Mollard, reporting one 'exceptional' case of selective basal collapse, is less pessimistic on the whole, but still very apprehensive of adhesions and even of contra-selective development of artificial pneumothorax (which latter incident, by the way, we have never seen).

(3) Rubin reports as 'unusual' two cases of selective collapse of the lower lobe.

#### Case reports

The following seven cases of basal tuberculosis, which we found among 444 tuberculous patients (= 1.6 per cent) during the last four and a half years, attracted our attention, because artificial pneumothorax treatment not only succeeded without exception but became conspicuous by the selective collapse of the affected base. In six cases the right base was affected, in one the left. Two were male patients, and five females. The average age of all patients was 21 years. The diagnosis was confirmed in each case by the presence of tubercle bacilli in the sputum. The topographical conditions have been already dealt with earlier in this article. Further details of our observations are given here. For brevity, irrelevant data are omitted. (Each illustration bears the number of the corresponding case, the picture *a* showing the condition before artificial pneumothorax

treatment, and the picture *b* after artificial pneumothorax treatment.)

*Case 1* (figures 1a and 1b, plate III), Hindu female, 19 years, suffering since about February 1943 from cough, expectoration, and fever. Admitted on 3rd May, 1943, showing in x-ray examination a *confluent infiltration of the whole right base, the exterior part being denser than its connection with the hilar shadow*. Distinct int. . . . . There are various vague, small . . . . . centre of the opacity, suggesting . . . . . a slight hæmoptysis on the day of her admission. Artificial pneumothorax on the right is established the following day and continued by routine methods. X-ray screenings and the last photo of 26th July show a complete pneumothorax with selective collapse of the base. The photo, as well as the screenings, suggests the collapse of two basal lobes in a sort of atelectatic way, whereas the two other lobes appear healthy and transparent. The patient is improving remarkably in every respect. As the sputum is still positive, phrenic-interruption will probably be resorted to.

*Case 2* (figures 2a and 2b, plate III), Hindu female, 26 years. Admitted on 21st May, 1942, after suffering for about two months from cough, expectoration, and fever. X-ray examination shows a condition similar to case 1, with round, 'punched-out' cavity of over a rupee's size near the dome of the diaphragm. Artificial pneumothorax of the right side is established the following day. Already after three refills the formation of a selective basal collapse becomes evident. On 2nd June the artificial pneumothorax treatment is supplemented by phrenic interruption at the right side. The patient improves rapidly. Subsequent ambulatory refills are continued without any complications.

*Case 3* (figures 3a and 3b, plate III), Mohammedan female, 19 years. Admitted on 13th April, 1940, after two months' illness. General condition very poor. Evening temperature between 101 and 102. X-ray examination shows *para- and retro-hilar condensation at the right side extending along the lesser fissure ('cortico-pleurite' of the French). Confluent, cloudy infiltration of the right triangle*. It is impossible to find out whether the basal lesion is older. There are admittedly strong points in favour of a mere basal aspiration secondary to the hilar lesion. The whole aspect, however, is rather atypical for an ordinary tertiary process, so that a basal onset with a hilar reaction is an equally possible interpretation. Artificial pneumothorax treatment, established on 17th April, results again in a typical selective collapse of the affected basal parts. The small air space is not recognizable in photo 3b, but is marked in the key diagram. The selective collapse, however, of the distinctly outlined lower lobe is quite evident. After short improvement, the patient discontinues the treatment three months later, against medical advice.

*Case 4* (figures 4a and 4b, plate IV), Hindu female, 18 years. Admitted on 7th June, 1941, in extremely poor condition after four months' suffering from cough, expectoration, fever and diarrhoea. The photo shows *dense, confluent infiltrations extending from the hilar region into the central and interior parts of the base*; there are several 'moth-eaten' transparencies suggesting cavitation. Moreover, there is a tuberculous dactylitis of the left fourth finger. Very suggestive signs and symptoms of intestinal tuberculosis make the outlook still more gloomy. Without much hope, artificial pneumothorax of the right side is established on 17th June. After a few refills a typical selective collapse of the base is obtained in spite of a diaphragmatic adhesion. The patient, however, develops fresh foci in the opposite lung; the intestinal disorders grow worse. After two months of treatment, she is taken home by her relatives in a moribund condition.

*Case 5* (figures 5a and 5b, plate IV), Hindu female, 19 years. Admitted on 30th October, 1941, in

poor condition after three to four months' illness. The photo shows *dense consolidation of the interior two-third of the right base conspicuous by its massive fusion with the hilar shadow*. Large, irregularly shaped cavity in the centre of the right base. Dense, bronchopneumonic outspread in the left middle zone. On 1st November artificial pneumothorax is established at the right side with early attainment of a selective collapse of the affected lobe (lower lobe?) and disappearance of the cavity within three months. There is a slight pleural effusion one and a half months after the artificial pneumothorax induction, being absorbed without any interference in the course of the following four to five weeks. A contralateral artificial pneumothorax is induced six weeks after the first one, our second photo showing the bilateral artificial pneumothorax condition four months after admission. At that time the patient has remarkably improved, and is discharged at her request for further ambulatory treatment.

Case 6, Hindu male, 26 years. Admitted on 26th July, 1940, after suffering for about three months from cough and expectoration. The x-ray photo showed *nodular (fibro-calcious?) infiltrations radiating downwards from the very opaque right hilar region with great (2" : 2") cavity near the lower pole of the hilum*; some scattered fibroid lesions in both upper lobes. Artificial pneumothorax treatment is established on 29th July, resulting after two further refills in a selective collapse of the affected lobe (lower lobe?). Within two weeks, remarkable improvement in every respect. In x-ray examination, the cavity has become almost invisible. The patient insisted on going away for further treatment, unfortunately taking his x-ray photos away.

Case 7 (figures 6a and 6b, plate IV). Hindu male, 19 years. Admitted on 10th November, 1941, in very poor condition. The photo shows a *huge cavity occupying the centre of the left base close to the lower pole of the hilum*, surrounded by patchy infiltrations; scattered patches with several irregular, annular shadows throughout the right middle and basal parts. To give the patient a chance, artificial pneumothorax is established at the left side on 12th November. Within the following three months, slow formation of selective collapse of the left lower lobe. Although the shape of the cavity becomes flattened and elongated, its size does not decrease, probably due to adhesions at the perpendicularly opposite parts of the lobe. A contralateral artificial pneumothorax started on 20th December, although complete, fails to arrest the deterioration of the right side. After five months the patient is now slowly sinking with signs of intestinal tuberculosis. He is discharged in rather a hopeless condition.

### Discussion

Five out of seven cases had unquestionable benefit from the treatment. The two other cases arrived in already an advanced and toxic condition, with complications such as intestinal and bone tuberculosis. But even these latter cases showed selective collapse of the affected parts, thus emphasizing the very point we wish to demonstrate. We could find none of the apprehended complications of other authors, such as extensive diaphragmatic adhesions, contra-selective collapse, early adhesive and thickening pleurisy: we could find no particular difference in basal lesions in different sites. From the mechanical point of view, all three above-mentioned types reacted equally favourable to artificial pneumothorax treatment. Against earlier opinions, however, we wish to emphasize quoting Rubin (1937) '... that a selective

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## GIARDIASIS

By RUDOLF TREU, M.D., L.R.C.P.

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In recent years, giardia infestation is increasingly gaining the interest of observers in this country and elsewhere. The widespread distribution of this protozoon in man has always been appreciated, but it appears that neither the almost unlimited variety of symptoms caused by this protozoon nor the fallacies in tracing these symptoms back to their real cause have yet been sufficiently realized.

Whatever the reason may be, it is certain that in the limited field of my practice I am seeing amongst the same class of patients a far greater number of giardia infections than could be

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pneumothorax cannot be attained through any particular skill on the part of the physician. The determining factors are beyond his control. Once a selective pneumothorax establishes itself, it is generally desirable to maintain it. This can be done simply by following the universally accepted rules in artificial pneumothorax treatment. Forceful collapse of expansible healthy lung tissue is nowadays generally rejected as being more harmful than good. On the other hand, should healthy lobes in time become adherent to the chest wall, no damage is done as long as the collapse of the affected part can be maintained.

Although the number of our observations is but small, the constancy with which a selective artificial pneumothorax was established seems to be more than a mere coincidence.

### Summary

Three topographical types of basal tuberculosis are discussed.

Seven cases are reported in which artificial pneumothorax treatment brought about selective basal collapse.

### Acknowledgment

I am indebted to Dr. H. Mollard, M.D., for his personal communication of unpublished data, and to Dr. V. P. Trivedi, M.B., B.S., Jamnagar, for his photo-technical assistance.

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observed during the years before the war. At that time, giardia infestation as the sole cause of a particular gastro-intestinal upset was not a common diagnosis in India. In European countries the infection was practically unknown then, and consequently when it occurred it was only too often overlooked (Dibold, 1935).

The scant attention paid to giardiasis is reflected by the fact that Manson-Bahr (1940) in his textbook devotes only  $1\frac{1}{2}$  pages to this infection. Discussing the symptomatology of giardiasis he does not mention that giardia may be the cause of typical dysentery attacks with bloody, frequent stools, though the stool may contain mucus at times when numerous vegetative parasites are found. The similarity of the symptoms caused by giardia with those caused by sprue is stressed by Manson-Bahr. This clinical picture was again described by Chaudhuri (1943) recently. It certainly is one of the common manifestations of giardiasis.

How markedly opinion is still divided as to the symptoms of giardiasis becomes evident from the report on the Meeting of the Section of Medicine of the Royal Academy of Medicine in Ireland at which FitzGerald (1943) observed that giardia were likely to be absent if blood was present in the stools in any quantity. Ruge (1930), however, observes that, particularly amongst children in tropical climates, giardiasis appears not uncommonly as a typical dysentery; sometimes even it may produce a picture closely resembling cholera.

The periodicity of symptoms in giardiasis is pointed out frequently. Also the fact that giardiasis may produce almost any combination of abdominal symptoms, sometimes leading to unnecessary operation; even the suspicion of tuberculosis and subsequent treatment in lung sanatoria has been described (Dibold). However, amongst the large number of hospital patients examined within two years, Dibold observed only 11 cases of giardia infection, a number which is certain to be very much below the findings in India amongst an equally large group of patients.

Perhaps insufficient attention has been paid to the great difficulty experienced at times in establishing a diagnosis. This is illustrated by the following case:—

On 15th October, 1942, I was consulted by a male European, 51 years old. His complaints began 6 years before: there was a typical periodicity—for periods ranging between 2 to 4 weeks he felt fairly well though never quite fit during these years. His stools were regular and there was hardly any abdominal discomfort. At the end of such a normal period he became constipated, this constipation lasting several days. Then he would suddenly, usually at night, start vomiting, have many and astonishingly large motions which were first formed, later loose. This period of diarrhoea lasted usually 2 or 3 days. During this time he was utterly exhausted, almost in a state of collapse and quite unable to leave his bed. There was never any pain. In August 1941 he underwent hospital treatment. All routine examinations were done with negative results. Radiologically there was a suspicion of ulcer in the

duodenum, so he was given Sippy treatment, which added to his exhaustion.

Some months afterwards, while his symptoms persisted, his gall-bladder was x-rayed and found to be very large and ptotic. Treatment with cholagogues brought no improvement, and when the patient consulted me he felt very exhausted and hardly fit to work. He had lost a good deal of weight.

On examination the patient showed no obvious abnormalities apart from a mild degree of anaemia. The radiological examination of the gastro-intestinal tract showed enteroptosis, but no evidence of duodenal ulcer. The outstanding fact of interest was the particularly slow evacuation of the large intestine which even after 5 days still showed large amounts of barium in the descending colon. Five days after the barium meal it could be observed also that the caecum and ascending colon contained very large amounts of faecal matter. The proximal part of the colon was extremely distended. Obviously the patient was heading for another of his attacks. It was now two weeks since the last attack of copious diarrhoea. His stools contained no protozoa and only *B. coli* could be detected on plating. (This, he stated, had been the case also at numerous examinations previously.)

As there was no other obvious cause for this recurrent upset, I treated the patient with carbachol, prostigmine, and vitamin B<sub>1</sub>, assuming the cause to be a vegetative neurosis although there were no other neurotic stigmata. The next attack was delayed for some time, but on 17th November there was another attack, of milder character. The patient did not have to go to bed. Another attack, at first quite mild, developed on 11th January, 1943. This attack became severe in the early hours of 12th January; there was a good deal of vomiting and very copious stools. Stool examination again showed neither protozoa nor pathogenic bacteria. In February 1943, there was again a mild attack of diarrhoea, without the feeling of exhaustion; in March, April and May there were again attacks, all comparatively mild. The patient felt that the treatment, though not quite successful, had improved him considerably.

On 12th May, while there was again a mild attack of diarrhoea, for the first time I found very numerous giardia cysts. These cysts had never been seen before by me nor by two pathologists to whom the stools also had been sent during previous attacks. The patient now remembered that giardia cysts had once been found in 1940. The attending physician had not paid much attention to this.

Treatment was instituted at once with quinacrine in the usual manner, 3 tablets daily for 5 days, and the patient has felt perfectly well ever since. He has put on weight, his stools are regular, and he feels fit again. But his giardiasis may not be cured yet. On 24th May as well as on 23rd July there were a few motile giardia in his stool, no cysts.

This puzzling observation, that quinacrine cures the symptoms of giardiasis rapidly but does not always eradicate the infestation, I have made repeatedly. A very significant case in point is the following:—

A European boy, 8 years old, suffered for one year from almost typical sprue symptoms and had been treated for sprue. He had lost much weight and passed every day 4 to 6 very large, pale white stools. The stools contained microscopically much fat, chiefly fatty acid crystals. The microscopical report on his stool was 'a few entamoeba histolytica cysts, no giardia'.

Three days after the first stool examination I examined the stool myself and found it swarming with giardia, chiefly cysts, but also motile forms. The number of giardia was so enormous that I asked the pathologist to come and have a look himself, the difference between his report and my findings being so astonishing.

With quinacrine there was an immediate improvement and there have never been more than 2 small stools per day since. For the first time for a year the boy has also put on weight, and his general condition is



greatly improved. Nevertheless, I still found motile giardia and occasionally cysts repeatedly, even after a second quinacrine treatment.

The observation that giardia may be swarming in a stool one day and none be found the next day is apparently not rare.

On July 1943, I was called to see an Indian boy of three years of age who was passing blood and mucus with frequent stools for two days. There was also slight fever. The laboratory report was: 'stool swarming with giardia, no pathogenic bacteria on culture.' When I examined the stool the next day there was not a sign of any blood or mucus, and I was unable to find a single giardia. On subsequent examinations no further giardia were ever seen. After this one attack, the boy has remained well. He has been given quinacrine (the treatment began after I had found the stool already negative).

These acute attacks of giardia dysentery appear to subside commonly without specific treatment. They also may occur again after a latency of many months and without connecting symptoms whatsoever. This type of giardiasis I have had occasion to observe repeatedly. In one case there was a latency of two years, when the patient, a boy of three years, had a comparatively mild attack. The next attack, two years later, was very severe. Within a very short time the boy passed large amounts of stool resembling raspberry jelly which on examination consisted almost entirely of motile giardia and red blood corpuscles. Atebrin was not available at that time. The patient was treated purely symptomatically; he was well within a few days and has remained so for more than three years. The enormous number of motile giardia in this case was very impressive. The large intestine must have been filled with giardia which must have multiplied at an incredible speed within a very short time, only to disappear again almost as suddenly.

Typical dysentery symptoms are much commoner in children than in adults, but in adults, dysentery-like symptoms are not as rare as one might expect from the study of the literature. Usually this type of giardiasis appears to be self-limiting. During the last few years I have not relied on this expectation but have preferred to administer active treatment with quinacrine. In one case of this type, the dysentery symptoms disappeared promptly, but not the infestation. Motile giardia were still present in small numbers even after two full courses of quinacrine.

It is not the object of this paper to describe in detail all possible manifestations of giardiasis. It may suffice to say that in every case of abdominal discomfort, flatulence, diarrhoea, steatorrhoea and dysentery, giardiasis as a possible cause will have to be considered. The giardia may be much more elusive than is generally assumed, and therefore, if no other cause can be found, single stool examinations cannot be relied on.

Authoritative statements on the pathogenicity of giardia are still conflicting. The textbook descriptions of this infection can hardly be said to be complete [5 lines on the symptomatology

appear in Price's textbook, not mentioning the occurrence of dysentery or sprue-like symptoms] and therefore it is not surprising that in general practice many cases are overlooked, and giardiasis is still regarded by many as a rarity.

In the following lines an attempt is made to bring into line the contradictory views on this infestation and to classify the different forms in which it may appear.

Giardia infestation presents itself in three different types. It is an interesting, although at the present state of our knowledge somewhat idle, question whether there are possibly several sub-species of giardia also.

(a) The common appearance of giardia in the stool of normal subjects is without clinical interest. This type is seen frequently in children and adults.

(b) Heavy infestation of the *colon* may produce symptoms indistinguishable from those of dysentery; this is commoner in children than in adults; motile giardia are present in the faeces. This heavy infection does not usually become chronic. It is usually self-limiting. It may originate from type A when for some unknown reason the giardia suddenly multiply enormously in a subject who showed no symptoms previously, possibly for a long period; or it may originate in a freshly infected subject in whom the giardia finds a particularly good soil for this rapid multiplication.

(c) The infestation of the *small intestine* shows a greater tendency to chronicity. It may last for many years. This type of giardiasis, often characterized by periodicity of symptoms, is apparently very amenable to treatment with quinacrine. With the disappearance of symptoms the cysts which are found in this type of giardiasis usually disappear too, but it is not uncommon for motile giardia to persist even after repeated courses with quinacrine.

Quinacrine, therefore, cannot be said to be a specific in the sense that it destroys all giardia. It certainly diminishes their number to such an extent that clinical symptoms disappear. In the usual dosage, however, it does not always destroy all the giardia in the colon.

#### Summary

Several cases of giardiasis are described, illustrating the different manifestations of giardiasis. One case, suffering for six years from periodic attacks of diarrhoea with loss of weight and increasing debility, is cited to demonstrate the difficulty of diagnosis.

An attempt is made to classify giardia infestation as:—

(a) Infestation without clinical significance.

(b) Massive infestation of the colon, with symptoms of dysentery, more commonly seen in children (motile forms in the stool).

(c) Infestation of the small intestine with a great variety of symptoms, usually, but not

(Concluded on opposite page)

## AMOEBIASIS WITH SPECIAL REFERENCE TO COMMON SECONDARY MANIFESTATIONS IN THE PUNJAB

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### Introduction

EXTENSIVE surveys of carriers of *Entamoeba histolytica* have not been attempted in India. Available civil and military records indicate an average carrier rate of about 20 per cent. This figure may be too high for some parts of India and too low for others, but epidemiological data are in accord with the clinical observation that in the Punjab undoubted amoebic lesions occur with a frequency which makes amoebiasis a problem of great importance. Existing knowledge on amoebiasis consists of a great many facts and not a few fancies. The object of this article is to lay stress on clinical facts which, the writer believes, are too often forgotten, and to warn the practitioner against beliefs which have little scientific foundation.

### Clinical considerations

Clinical manifestations of amoebiasis are dependent upon the primary localization of the amoeba in the gut, on secondary localization due to direct invasion of neighbouring tissues, and, very rarely, on the invasion of the blood stream and involvement of distant organs.

### Primary amoebiasis

Primary amoebiasis consists of two distinct clinical groups :—

1. Acute amoebic dysentery, which comprises not more than 10 per cent of cases (Knowles).
2. Chronic amoebiasis or a non-dysenteric carrier state constitutes 90 per cent of cases of amoebiasis. Clinically this group may be divided into three sub-groups :—

(a) Cases showing no symptoms.

(Continued from previous page)

exclusively, seen in adults (stools usually presenting cysts).

Quinacrin is recognized to cure the symptoms of infestation. It does not always cause disappearance of all giardia, particularly of motile giardia, from the colon.

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(b) Cases showing constipation with occasional looseness of the bowels and abdominal discomfort.

(c) Cases with or without abdominal symptoms which show marked constitutional disturbance usually attributed to allergic states and focal sepsis.

What is the exact percentage of these groups and sub-groups, and how far the constitutional symptoms can rightly be attributed to primary amoebiasis, are questions which are open to controversy, but there is little doubt that some of the accounts in the existing literature, which attribute almost any physical or nervous state to amoebiasis, indulge more in fancy than in fact. It must be remembered that even the presence of the *Entamoeba histolytica* in the stools is not a positive proof of its aetiological relationship to every symptom shown by the patient, and it is not surprising that amoebicidal drugs often prove disappointing, because they are prescribed on inadequate grounds. The carrier constitutes one-fourth to one-fifth of the human population, and is subject to the usual physical and nervous ailments of mankind. Although current literature shows a swing in favour of the old view that amoebic dysentery is the more prevalent type of dysentery in some parts of India, the fact must not be overlooked that bacillary dysentery is a major cause of bowel trouble which, in common with many other bowel complaints, may cause symptoms similar to those of amoebic dysentery. Statistics may at times mislead, but if the practitioner looks upon each case as a problem for clinical judgment and full investigation, they can do little harm.

### Secondary amoebiasis

Secondary amoebiasis is associated with symptoms of localized suppuration in connection with various tissues and organs of the body. Every carrier of *Entamoeba histolytica* is a possible sufferer from these serious complications. The frequency with which they occur is not sufficiently realized by the practitioner. The writer has included an account of seven cases which presented problems of diagnostic importance. Cases 1 to 6 came under his observation during a period of about one year at the V. J. Hospital, Amritsar, and case 7 at the Mayo Hospital, Lahore.

### Pathological considerations

What is the significance of the *Entamoeba histolytica* in the stools? We are unable to give a definite reply to this question. Some believe that *Entamoeba histolytica* may occasionally live a harmless saprophytic existence in the lumen of the gut. Others postulate a non-pathogenic strain of the *Entamoeba histolytica*. The consensus of opinion appears to be that the presence of *Entamoeba histolytica* in the stools is invariably associated with the presence of microscopic or macroscopic ulcers in the wall

of the cæcum, the sigmoid being involved in the vast majority of cases in later stages. Such ulceration, however, is often not associated with dysenteric symptoms, the latter being the end result of progressive ulceration dependent upon such factors as lowered vitality of the intestinal tissue, the virulence of the strain of *Entamoeba histolytica* causing the infection, or the synergistic action of other organisms such as the hæmolytic streptococcus or the dysentery bacillus. Two important points to be borne in mind are that extensive amœbic ulceration may be associated with no dysenteric symptoms, and dysenteric or other constitutional symptoms may have a non-amœbic origin in carriers of the *Entamoeba histolytica*. The subsequent course of the disease depends upon two factors :—

1. Absorption of bacteria and bacterial products, and unchanged or partially digested food from the ulcers, giving rise to toxic, septic or allergic disorders.

2. From the primary lesion in the gut the amœba may travel in one of three possible directions giving rise to secondary amœbiasis :—

- (a) Invasion of the portal system gives rise to amœbic hepatitis. The inflammation may subsequently spread to the lung by direct continuity.

- (b) Direct spread through the muscular and peritoneal coats of the intestine gives rise to abscess round the appendix, the kidney, the rectum and the bladder.

- (c) Invasion of the systemic circulation and infection of the lung, brain, spleen, and possibly other viscera. This is a rare mode of spread, and most cases show simultaneous disease of the liver.

Experimental infection provides incontrovertible evidence of the pathogenicity of the *Entamoeba histolytica* in the kitten, which appears to be the most susceptible animal. Lesions can be produced in the wall of the gut, and portal invasion with hepatitis tends to occur, but there is no evidence of systemic invasion, and lesions in other organs do not occur; the liver acts as an efficient filter for the *Entamoeba histolytica*. In spite of differences in the pathology and life history of the amœba in the kitten, there is an obvious parallel and a possible explanation for the fact that, in the human being also, the portal system is often, and the systemic circulation rarely, invaded by the amœba. Attempts to infect the kitten through any route except the gut have failed consistently. These experiments should damp the enthusiasm of those who look upon amœbiasis as a constitutional disease capable of causing local symptoms in any organ of the body, due to a generalized septicæmia.

A remarkable feature of the majority of cases of amœbiasis is the non-existence of active dysenteric symptoms, and at the most only a history of transient or mild bowel trouble in the past. Physical signs in the abdomen also rarely indicate much inflammatory reaction in the cæcum or the sigmoid colon. It is possible,

therefore, that secondary lesions occur more often in those cases in which there is no extensive inflammatory reaction in the gut; consequently the wall is vulnerable, the blood vessels are patent, and free movement of the amœba is possible. On the post-mortem table, however, one has often seen liver abscess complicating extensive ulceration of the gut with marked fibrotic change.

### *Amœbic hepatitis*

Amœbic hepatitis is the commonest secondary manifestation. According to Clark (Knowles, 1928) 51 per cent cases of amœbic dysentery on post-mortem evidence show hepatic involvement. There are few tropical diseases which are as well known and yet so often missed. The typical case with enlarged painful liver; fever and leucocytosis is rarely missed, but mistakes are made very often because one forgets that the typical clinical, laboratory and x-ray findings may be absent in amœbic hepatitis. Confusion is increased by the variable mode of onset and clinical course which may be acute, subacute or chronic. Acute and chronic abdominal as well as chest conditions can, therefore, be simulated by amœbic hepatitis. Clinically amœbic hepatitis may be divided into the following groups :—

1. *Latent hepatitis*.—In this group there is no obvious evidence of hepatitis, and fever and leucocytosis are absent. Castellani (1935) describes the following three physical signs in this type of case, which should be looked for :—

- (a) Percussion or pressure along the midline from umbilicus upwards results in pain immediately below the ensiform cartilage. In duodenal ulcer the pain is lower down in the same line and in cholecystitis towards the right.

- (b) Dullness on firm percussion at the junction of the mid-axillary line and a line drawn horizontally outwards from a point 4 cm. below the right nipple. The dullness extends outwards for some distance from this point.

Signs (a) and (b) should be elicited in the recumbent posture.

- (c) With the patient sitting up there is dullness of the right base and increased tactile fremitus.

He regards a combination of two signs as suggestive and of three signs as diagnostic.

This type of case is seldom recognized and passes on gradually to group 2 and then to 3.

2. *Subclinical hepatitis*.—In this group the presenting feature is often a pyrexia with leucocytosis, and local liver signs are insignificant, although tenderness can usually be elicited on pressure. This type of case is not uncommon; two case reports are included for illustration :—

*Case 1*.—A Hindu male, aged 15, was admitted with fever of two weeks' duration, remittent in type (100 to 104°F.), later assuming an irregular intermittent type. There was a history of diarrhoea one to two months previously. Some tenderness was noticed round the umbilicus and over the cæcum, but well-marked tenderness under the right costal margin on pressure

over the liver which was not enlarged. The general condition was good. The leucocyte count was 15,200 per c.mm.; polymorphs 72 per cent; eosinophils nil; no malarial parasites were found. The Widal test gave para A 1-60. Stools, urine and sputum were negative. The patient was put on emetine injections; the temperature dropped to normal within two days, the tenderness of the liver disappeared and the patient was free from symptoms for the rest of his stay in the hospital (one month).

*Case 2.*—A Hindu male, aged 25, was admitted with fever of ten days' duration and cough of two weeks' duration. There was a history of diarrhoea for one month previous to the onset of the fever. The spleen was palpable; the liver not enlarged, but tender on pressure; the caecum tender. Fever was irregular, remittent in type, ranging from 99 to 102°F. The patient showed toxæmia and had a 'muddy' complexion. The leucocyte count was 11,000; polymorphs 67 per cent; eosinophils nil. Hb was 80 per cent and the total RBC  $2\frac{1}{2}$  millions. The Widal test was negative. Two stool examinations and sputum examination gave negative results. No malarial parasites seen. On account of the enlarged spleen, the patient was put on quinine in full doses with no effect. A third stool examination showed *Entamoeba histolytica* cysts. Emetine injections were started. The temperature dropped to normal after the second injection and tenderness of the liver disappeared. The patient remained free from symptoms for several weeks as long as he was under observation.

3. *Classical hepatitis.*—This type of case shows enlarged and painful liver, fever and leucocytosis. This condition is common, is easily recognized and does not need any illustration.

### *Pulmonary manifestations*

In a case in the tropics, acute or chronic, where signs and symptoms point to disease in the lower right chest, amœbic infection of the liver, pleura or the lung must be kept in mind, especially if there is a recent or old history of bowel trouble. This is a simple rule which, if remembered, will prevent many mistakes. From the case reports given below it will appear that pulmonary complications of amœbiasis are not uncommon.

Pulmonary manifestations in secondary amœbiasis may be grouped as follows:—

I. Physical signs at the base of the right lung as a result of upward enlargement of the liver giving rise to compression of the lung. There is diminished air entry and sometimes a few crepitations. These signs, when present, constitute valuable confirmatory evidence of amœbic hepatitis. Where the diaphragm is considerably raised the heart is also appreciably displaced.

II. 'Hepato-pleural' amœbiasis:—

(a) Empyema due to rupture of liver abscess into the pleura. This is often an acute phenomenon.

(b) Dry exudative pleurisy, due to spread of inflammation from the liver.

III. 'Hepato-pulmonary' amœbiasis is due to adhesions between the diaphragm and the lung, the inflammatory process spreading directly to the lung tissue from the liver with or without obvious rupture of the diaphragm. Clinically

these cases usually show some evidence of disease in the liver also.

IV. 'Primary' pulmonary amœbiasis in which infection is conveyed from the gut to the lung through the blood stream. This group may not show clinical evidence of disease of the liver.

The writer considers that the terms 'hepato-pleural' and 'hepato-pulmonary' should be widely adopted because they depict the pathology of the disease accurately.

### *Case reports of illustrative cases*

*Case 3. Empyema due to rupture of liver abscess.*—A Mohammedan male, aged 55, was admitted in a state of collapse, with a history of fever and vague abdominal pain of two months' duration and an old history of dysentery. On the day of admission he had severe pain in the right chest, dyspnoea and cyanosis. The right chest was full of fluid. The liver was just palpable below the costal margin, and tender. There was œdema over right lower chest. The leucocyte count was 15,600 per c.mm.; polymorphs 81 per cent; eosinophils 20 per cent. Sputum, urine and stools were negative. X-ray taken two days before admission showed a definitely raised right diaphragm and clear lungs. X-ray after admission showed the right pleural cavity full of fluid and the heart markedly displaced. On aspiration, chocolate-coloured pus was recovered from the pleural cavity, confirming the diagnosis of liver abscess with rupture into the pleura. The patient died.

*Case 4. Abscess of the lung with empyema secondary to amœbic hepatitis.*—A Hindu male, aged 50, was admitted with pain in the right hypochondrium, intermittent fever, cough, with blood-tinged sputum, and dyspnoea, with considerable toxæmia. Symptoms started six weeks previously and became intense a few days before admission. There was an old history of dysentery. The right base showed evidence of consolidation; the liver was just palpable and tender on pressure. The caecum was palpable and tender. The patient had a scar in the epigastrium representing an operation for an abscess one year previously, presumably amœbic abscess of the liver. The leucocyte count was 17,000 per c.mm.; polymorphs 75 per cent; eosinophils nil. Sputum, stool and urine examinations were negative. W.R. negative. M&B 693 was given because the acuteness of the illness suggested a pneumonic condition. Temperature and symptoms continued. X-ray showed a diffuse opacity involving the lower two-thirds of the right lung. On aspiration  $1\frac{1}{2}$  pints of chocolate-coloured material was recovered from the pleura. The patient was put on emetine. The fever disappeared five days later, cough and expectoration gradually subsided and the general condition improved rapidly. The patient was later discharged free from all symptoms.

*Case 5. Amœbic abscess of the lung secondary to hepatitis.*—A Hindu male, aged 28, was admitted with chronic low irregular intermittent fever, cough, blood-stained sputum, and pain in right hypochondrium. There was a history of dysentery nine months previously. The general condition was good but the fingers showed clubbing. The right base showed impaired percussion note, distant breath sounds and crepitations. Liver and caecum were tender. Stools, urine and sputum examinations negative. W.R. negative. Total leucocyte count 14,000 to 20,000 per c.mm. on different occasions. A diagnosis of abscess of the lung was made and the patient put on M&B 693 with no response. X-ray showed diffuse opacity at the base of the right lung. On injection of lipiodol a condition of bronchiectasis was observed in the bronchi round about a diffuse opacity. On the basis of the history of dysentery, pain in right hypochondrium and tenderness of the liver which was not enlarged, the patient was put on emetine. The fever disappeared on the third day, expectoration and pain in the course of next week. There was no recurrence

of symptoms, and the patient was discharged six weeks later.

**Case 6. Pleural effusion complicating amœbic hepatitis.**—A Mohammedan male, aged 25, was admitted with fever and a large and tender liver. There was a history of dysentery three months previously. The general condition was good. The base of the right lung was stony dull. On aspiration, straw coloured fluid indistinguishable from that of a tuberculous pleural effusion was recovered. The leucocyte count was 6,500 per c.mm., polymorphs 70 per cent, eosinophils 1 per cent. Stool and sputum examination negative. The patient left hospital before investigation could be completed or treatment administered. Laboratory evidence is weak, but Manson-Bahr (1939) records absence of leucocytosis in 12 per cent of his cases of hepatitis. On clinical grounds a diagnosis of amœbic hepatitis with exudation into the pleura appeared fairly certain. If the liver signs were not definite a diagnosis of pleural effusion (tuberculous) would have been made.

**Case 7. Dry and exudative pleurisy and abscess of the lung following amœbic hepatitis.**—This is a very interesting case presenting the various types of pulmonary lesions following amœbic hepatitis.

A male, aged 28, was admitted with pain in the right chest, hæmoptysis, cough and expectoration, occasional fever up to 100°F., of two months' duration. Four months previously the patient (an educated man) reported that he had suffered from dry pleurisy followed by effusion and occasional looseness of bowels. Physical examination showed diminished air entry over the right base. X-ray showed an opacity with cavitation over the right base but no effusion. The right diaphragm appeared slightly raised. After one week's hospitalization the temperature settled down but, in spite of intensive sulphonamide therapy, continued to show occasional slight rises and the leucocyte count remained 16,000 per c.mm. After one month the patient still complained of pain and was passing hæmorrhagic mucopurulent sputum. The liver was just palpable below the costal margin, but definitely tender to pressure. The cæcum was tender and just palpable. Stool examination was negative. The leucocyte count was 12,500 per c.mm. Emetine injections were started. The quantity of sputum and the blood in the sputum steadily diminished, and the tenderness of the liver disappeared. After one week practically no expectoration and no blood in sputum. X-ray of lungs clear.

**'Primary' pulmonary amœbiasis.**—This group is admittedly small. It includes cases in which there is no involvement of the liver, and the lung lesion is due to invasion of the systemic circulation; no continuity can be established between the lesion in the liver and that in the lung. It is obvious that the 'primary' nature of the lesion can only be established post mortem, because during life hepatitis can be completely silent, and the question of disease in the liver in continuity or otherwise of the lesions cannot be settled without diligent dissection. Of course, if the lesion in the lung is so situated that anatomically it cannot be involved by direct spread of inflammation from the liver, the diagnosis may be made during life, but the majority of cases reported in the literature (including those by Manson-Bahr) are basal mostly in the right lung, suggesting the spread of inflammation from the liver.

One case of 'primary' pulmonary amœbiasis in the upper zone left lung was reported in the *British Medical Journal* (Dormer and Friedländer, 1941).

**Amœbiasis of brain and spleen.**—Undoubted cases of systemic invasion are reported. But the lesions are very rare. Most cases show simultaneous disease of the liver. The strictest morphological and even cultural standards must be satisfied before an amœba-like structure in suspected lesions is labelled as the *Entamœba histolytica*, because macrophage cells are extremely difficult to differentiate.

#### *Symptomatology of the present seven cases*

1. Fever was present in all cases, varying in height, remittent or irregular intermittent in type. Toxæmia as indicated by the general condition varied greatly, and was sometimes absent.

2. Rigors were not noticed in any case.

3. Liver signs. Marked upward or downward enlargement was noticed only in cases 3 and 6. In the rest, enlargement could not be made out clinically or was very slight. Pain in right hypochondrium was present in cases 4, 5 and 7. Tenderness on pressure of the liver was the most constant sign and was present in all cases. Pain in the shoulder was not noticed in any of the cases.

4. Intestinal symptoms and signs were insignificant in all cases, although a previous history of diarrhoea or dysentery was a constant finding. No demonstrable thickening of the colon was present except in cases 4 and 7. Some tenderness of the cæcum, however, was usual though not constant. Stools showed no *Entamœba histolytica* except in case 2, but not more than three examinations, often fewer, were done in any of the cases. Without attempting to defend the routine methods of examination of stools even in the larger hospitals, the writer has no hesitation in observing that, in spite of the impressive array of figures by the epidemiologist, the clinician is often faced with a negative stool report and the diagnosis frequently is purely clinical supported by the results of treatment. Occasionally a positive stool report but much more often a negative stool report will be misleading, if clinical, blood and x-ray findings are not taken into consideration. Castellani (1935) remarks 'in chronic amœbic colitis, diarrhoea with blood and mucus is often absent and stool examination day after day may be negative'. He refers to a case in which a positive stool result was obtained on the 90th examination. Sigmoidoscopy was not done in any of the reported cases.

5. Lung signs. Typical chocolate-coloured pus was recovered from the pleura in two cases. In the lung abscess cases, the sputum was mucopurulent containing a varying quantity of blood. It is possible that these patients coughed up typical anchovy-sauce sputum before they were hospitalized. The *Entamœba histolytica* was not found in the pleural or pulmonary discharges. Dry and exudative pleurisy and empyema were presented by cases 3, 4, 6 and 7.

6. Leucocytosis, 11 to 20 thousands per c.mm., was noticed in all cases except case 6. Only one



case showed polymorphs above 80 per cent (case 3). Eosinophilia was not met with in any of the cases.

#### *Diagnosis of latent and sub-clinical amoebic hepatitis*

When the liver is not apparently enlarged, but symptoms point to trouble in the lower right chest or the upper right abdomen, the possibility of amoebic hepatitis must be kept in view. In sub-clinical cases, the syndrome of fever, tender liver, a history of diarrhoea or dysentery is characteristic. Some confirmation is obtained by demonstrating leucocytosis which is almost constant. Repeated stool examinations and x-ray will help in other cases. It may be pointed out that this type of case sometimes finds its way into the tuberculosis wards on account of the association of fever with a dry cough.

According to Rogers (Rogers and Megaw, 1942), in endemic areas, unexplained fever with leucocytosis should be suspected as being due to amoebiasis even in the absence of a history of dysentery, of symptoms of hepatitis, and of *Entamoeba* from the stools.

#### *Diagnosis of amoebic hepatitis with enlarged liver*

When the liver is obviously enlarged and tender, differential diagnosis has to be made from other diseases causing a similar change in the liver. In particular, mention may be made of chronic malaria and chronic venous congestion of the liver, both common conditions, which are apt to be mistaken for amoebic hepatitis. Chronic malaria should always be suspected when an enlarged spleen is associated with enlarged or tender liver.

#### *Diagnosis of pulmonary amoebiasis*

In any pathological condition of the base of the right lung or of the right pleura, pulmonary amoebiasis must be considered in diagnosis. The syndrome described in amoebic hepatitis is almost invariably present because lung disease is usually secondary to liver disease. In addition, pulmonary or pleural signs will be present. Pulmonary tuberculosis involving the base, bronchiectasis, foreign body in right bronchus, malignant disease, syphilis, unresolved pneumonia, avitaminosis, pleural effusion (tuberculous) and empyema are to be considered in differential diagnosis. The diagnosis of the rare 'primary' type is difficult during life and should be suspected only when any other diagnosis does not seem feasible. The *Entamoeba histolytica* can rarely be demonstrated in the sputum, and the greatest care should be exercised in diagnosis even when an amoeba-like structure is met with. The presence of *Entamoeba histolytica* in the stools is suggestive but not diagnostic. It should not be forgotten that pain, impaired percussion note, and diminished breath sounds over the base of the right lung due to amoebic hepatitis may simulate disease of the pleura or the lung, more

often the former. This mistake may possibly account for the early pleural manifestations of case 7.

#### *Treatment*

Emetine was given in six cases. Except in case 1 which was in a hopeless state from the beginning, the response was dramatic. The fever disappeared rapidly in all cases and other symptoms within a week. A single course of 1 gr. per day for one week was given except in case 1 in which  $\frac{1}{2}$  gr. per day was given. Although case 4 remained free from symptoms after the first course, a course of 7 injections was repeated four weeks after the first course in view of the severity and duration of his disease. Aspiration of pleura was done in cases 3 and 4. Clinical improvement under emetine may not be considered as proof of the amoebic nature of the disease process, because emetine is said to influence favourably congestive and hæmorrhagic states. Case reports appear in literature in which emetine influenced favourably the course of non-amoebic abscess of the lung, but when the effect is as striking, prompt and permanent as in cases cited above, the result of emetine therapy may be regarded as of diagnostic importance. Furthermore, the writer noticed no improvement in two cases of non-amoebic abscess of the lung treated by him with emetine.

#### *Summary*

1. Although exact figures of amoebic infestation amongst the various sections of the population are not available in India, there is little doubt that amoebiasis is widespread. The frequency with which undoubted secondary lesions such as amoebic hepatitis and pulmonary amoebiasis are met with in medical practice in the Punjab is a reliable guide to the incidence of amoebic disease of the bowel in the absence of accurate epidemiological data. There is, however, little justification for incriminating the amoeba for every obscure illness of mankind.

2. The classical type of amoebic hepatitis with enlarged liver is easily recognized. Latent and sub-clinical hepatitis, pleural and pulmonary lesions, are both readily missed. An account is given of seven cases which presented diagnostic problems of interest, all seen within one year.

3. 'Hepato-pulmonary' amoebiasis in which inflammation spreads directly from liver tissue to the lung tissue is the commonest type of lung lesion.

4. A reference has been made to surgical manifestations of amoebiasis in the abdomen due to direct spread of the amoeba through the wall of the gut to the surrounding tissues.

5. Secondary amoebiasis as a result of invasion of the systemic circulation is very rare. This group includes 'primary' pulmonary amoebiasis, amoebiasis of the brain and the

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## CANCER OF THE PENIS IN A CHILD AGED TWO YEARS

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Madras

In India, information regarding the incidence of cancer is very incomplete. Patients frequently present themselves at an out-patient department in an inoperable condition and are therefore not admitted. Hospital in-patients records are therefore very unreliable; some valuable information is available from out-patient departments.

One attempt was made by the author to carefully classify, record, index, and photograph with pathological reports of conditions that were inoperable in the out-patient department. Cases that were operable were admitted and treated.

(Continued from previous page)

spleen. No reference has been made to amœbiasis of other organs because the amœbic nature of lesions reported in the literature has not been established beyond doubt. Some of the reported cases appear to be due to faulty standards of identification of the *Entamoeba histolytica*, or to disregard of the fact that the amœba may travel through the wall of the gut and attack any of the surrounding organs without invasion of the blood stream.

6. The pathological principles underlying the various manifestations of amœbiasis have been discussed. In view of the fact that pleural and pulmonary lesions are almost entirely secondary to liver disease, it has been suggested that the terms hepato-pleural and hepato-pulmonary amœbiasis should be widely adopted for a proper appreciation of the pathology of these complications.

### Acknowledgments

My thanks are due to Major S. M. K. Mallick, I.M.S., whose opinion was solicited in the investigation of case 4, to the Director, Central Research Institute, Kasauli, for supplying one of the references, and to Dr. Amar Jit Singh, of Patiala, for supplying information relevant to the carrier rate in the Punjab on the basis of work carried out by him.

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The result of this was a classification of 335 cases from 1932 to 1934 (Kini) of which 52 were cancer of the penis. In the 52 cases of cancer of the penis classified (Kini and Rao, 1937), all were found among the Hindus. No case was found among Mohammedans. The average age at which the disease manifested itself was 45.3 years. The youngest was 35 years and the oldest 60 years.

In children, very few cases of carcinoma of the penis are described; Creiti described a typical embryonal carcinoma of the corpus cavernosum in a child aged 2 years. Curtis refers to a case of Weir's at the age of 18. Freyer reports a case in a boy of 17 (Herman, 1938).

The following case is interesting as it resembles the case described by Creiti. This was not included in the classification published, as it was seen in 1936.

In 1936, a child aged 2 years was admitted for a swelling in the lower part of the penis behind the tip, with a duration of two months. The mother said that she first noticed a small swelling on the dorsum of the penis behind the tip. The swelling began to grow rapidly, causing difficulty in passing urine with dribbling of blood from the tip of the penis, for which the child was brought to the hospital for treatment.

On admission the child was found to be irritable; the penis was fusiform in shape (see figure 1). The prepuce was stretched over it



Fig. 1.—A photograph of the penis at the time of admission.

with a blood-stained discharge from the tip of the penis.

The swelling felt firm and indurated. On exploration with a probe through the meatal opening, a small papillary growth was seen to protrude through it. The glands of the oblique chain in the left groin were enlarged and fixed,

and in one spot were adherent to the skin. On the right side, glands were palpable and were not adherent to the skin (*see figure 2*).



Fig. 2.—Showing the post-operative result of the amputation of the penis. Note the enlargement of the inguinal glands on the left side.

Under ethyl chloride-ether-oxygen sequence, a supra-pubic cystotomy was done and the bladder was drained with a Malecot's catheter. A partial amputation of the penis was done at

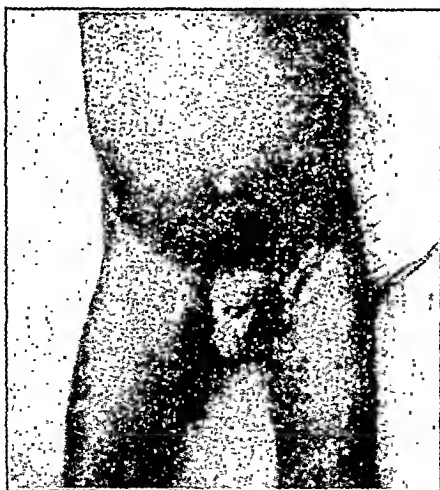


Fig. 3.—Illustrates the post-operative condition of the block dissection of the glands on the right side and effective radiation on the left side.

the root of penis, using a dorsal flap. The specimen (*see figure 4*) was sent for pathological examination.

Fifteen days after the operation, the glands on the right side of the groin were removed by block dissection. The glands on the left side were irradiated by the interstitial method, as they had become fixed to the skin and the deeper tissues. A total dosage of 1,368 mgm. hours was given. The child made an uneventful recovery, the glands on the left side disappeared and responded well to the irradiation (*see figure 3*).

*Pathological report.*—Dr. T. Bhaskara Menon, Professor of Pathology, Andhra Medical College,

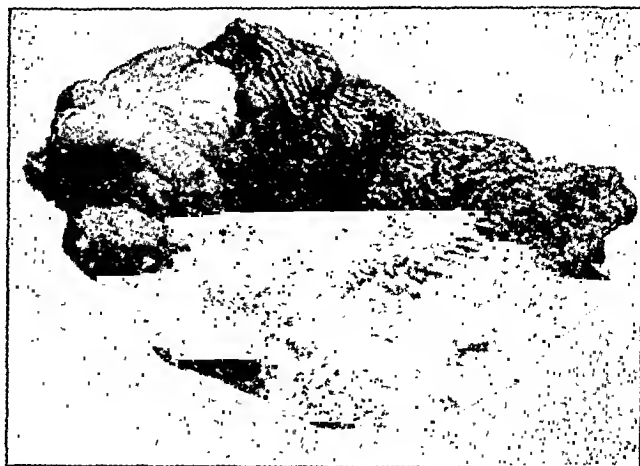


Fig. 4.—A photograph of the specimen that was removed, showing the involvement of the glands and lack of infiltration of the prepuce. The surface is not ulcerated but forms nodular elevations on the glands.

Vizagapatam, described the specimen as follows :—

'This is a nodular growth of the penis involving the glans. There is no ulceration on the surface of the glans, but there are nodular elevations of the size of



Fig. 5.—A histological section showing the adenopapillomatous type of the growth (H & E X 80).

a pea. The prepuce is not involved and the coronal sulcus is free. The urethral opening is in a depression that is surrounded by small nodules. On section the whole of the body of the glans and the corpus spongiosum are filled with soft greyish friable growth showing cystic areas and areas of hæmorrhage. The growth extends back for about 1 inch from the external meatus. The frenum and mucous membrane are not involved.

Histologically the growth is a papilliferous carcinoma forming cystic spaces and gland-like alveoli. The epithelial lining is varied; in places it is low columnar in type, in places cuboidal; it is frequently flattened and occasionally transitional in type, with several rows of cells. There is neither mucous formation nor stratification. The most noticeable feature is the tendency to form papillary buds (figures 5 and 6) as in

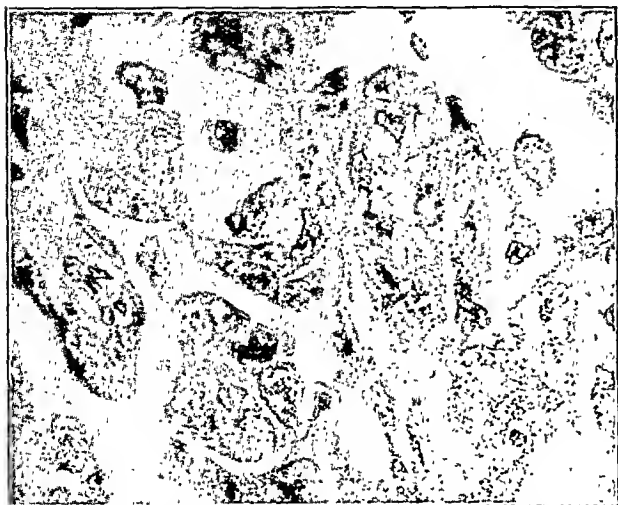


Fig. 6.—A histological section showing the variability of the epithelium and the formation of small papillary buds (H & E  $\times 600$ ).

the ovarian serous cystadenoma. There are numerous mitotic figures. The walls of the cavernous spaces are infiltrated with the growth. There is also a resemblance in some areas to the papillary carcinoma of the bladder. The situation of the growth so far forward and the absence of mucus forming epithelium rules out an origin from Cowper's glands which are the commonest sites of adeno-carcinoma of the penis. The lack of involvement of the coronal sulcus is against an origin from Tyson's glands. The variability of the lining epithelium suggests an origin from the urethral glands of Littre.

*Follow up.*—No reply has been received to letters sent yearly from 1937 to 1943, but the letters have not been returned by the Dead Letter Office. For the purpose of this report, it is presumed that the child must be dead.

*Points of interest.*—1. Carcinoma of the penis in children is very rarely reported. This is one of the very few cases and may be the second recorded in the literature.

2. This growth is a papillary growth infiltrating the walls of the corpus spongiosum. Tyson's gland as the possible origin of the growth has been ruled out due to lack of involvement of the coronal sulcus. The variability of the lining epithelium suggests an origin from the urethral glands of Littre.

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## OBSERVATIONS ON A 24-HOUR RAT TEST (ASCHHEIM-ZONDEK MODIFICATION) FOR THE DIAGNOSIS OF PREGNANCY

By D. W. SOMAN

*Haffkine Institute, Bombay*

THE efficacy of the Aschheim-Zondek test as well as its Friedman modification in the diagnosis of pregnancy is firmly established, and the present communication is not intended to appraise its value. These tests, however, suffer from a drawback in that the results of the tests are not available till the end of 96 and 48 hours respectively. Even to a most experienced obstetrician, the clinical evidence presented by cases of temporary amenorrhoea, profuse bleeding, pelvic tumours, malignancy and acute abdominal conditions may be so baffling as to necessitate aid from the biological tests in coming to an accurate and rapid diagnosis before he decides to resort to any operative procedures. A rapid diagnosis is especially desirable in cases suspected of ectopic gestation, and in those conditions in which the termination of pregnancy is imperative for the safety and life of the woman. Zondek has put it well by saying that the ideal pregnancy reaction would be a rapidly performable chemical reaction, but so long as such a reaction is not available, the hormonal pregnancy tests or one of their important modifications must remain useful.

Ever since Aschheim and Zondek (Aschheim, 1930) and Friedman and Lapham (1931) developed their classical hormonal tests for pregnancy using the mouse and the rabbit respectively, attempts have been made to modify the original tests by using different laboratory animals and different quantities of urine to obtain reliable and rapid results. Brouha was the first to suggest the use of infantile male rodents, utilizing the changes in the seminal vesicles. Dharmendra (1931) suggested the descent of the testes in the male rats as a reliable index. Reinhart and Scott (1931) tried immature rats, mice, guinea-pigs and rabbits and came to the conclusion that the rat offered no advantage over the mouse. Mathieu and McKenzie (1931) made use of female immature rats, injecting only one animal with 0.5 c.cm. of urine twice daily for three days and examining the ovaries after 96 hours; they got accurate findings in 97 per cent of cases. Davis and Ferrill (1932) replaced immature female mice by immature female white rats from 25 to 30 days old. Only three such rats were used, of which two were utilized for the test proper and the third one acted as a control. The two rats were injected intraperitoneally with 1 c.cm. of urine, and all three rats were anaesthetized 96 hours after the first injection, and the ovaries were examined. They made an accurate diagnosis in more than 98 per cent of cases by gross examination of the genitalia. Kelso (1940), with

a view to economizing time for reading the results and to eliminating certain disadvantages of the original Aschheim-Zondek test or its Friedman modification, reintroduced the immature female white rat as the experimental animal of choice. It has been shown that an immature rat is equally responsive to the anterior pituitary-like sex hormone. Albino rats are readily procurable and are easy to handle and inject. They can stand repeated injections of urine without ill effects. Very few die as a result of injection or subsequent infection. Their cost is much less than that of a suitable rabbit.

The modification suggested by Richard Kelso has been tried here with minor variations; results suggest that it has distinct advantages over the original Aschheim-Zondek test or its Friedman modification. The material for the observations recorded in this paper was utilized from among samples of urine sent for the Friedman test by various hospitals and private practitioners in Bombay. During a period of three years, 200 samples were tested concurrently by using rabbit and rats as the experimental animals.

#### *Technique*

Six c.cm. of urine was injected on the first and second day into the marginal ear vein of a rabbit; 48 hours after the first injection, the rabbit's abdomen was opened under anaesthesia and the ovaries were examined. For the rat test, the method suggested by Kelso was followed, using four immature female white rats for each test, out of which two were used for 24-hour test and the rest for 72-hour test. When a large number of samples showed complete agreement between the 24-hour and 72-hour tests, the 72-hour test in rats was dispensed with, because the rabbit test served equally well as a subsequent check. Only two rats for the 24-hour test were, therefore, used for test proper, instead of four as suggested by Kelso.

Female white rats between 22 and 40 days old were used for the test. These rats were taken from the Haffkine Institute stock and usually weighed between 30 and 65 grammes. Rats reach their normal period of puberty only when they are 7 to 8 weeks old. Therefore, forty days appears to be a quite safe upper limit for producing premature developmental changes in the ovary by the hormone in urine. Rats over forty days old are likely to show spontaneous ovarian maturity and give false positive results.

Samples of urine were usually fresh morning specimens collected in a clean vessel. Catheterization is unnecessary. The addition of a preservative is not necessary unless the specimen has to be mailed to a distant laboratory. In that case, a drop of tri-cresol can be added for every 25 c.cm. of urine. Such preserved specimens do not lose their hormonal potency for at least six days.

Alkaline urines were slightly acidified. Turbid samples were filtered. The samples were kept in a refrigerator between the times of injections

but they were allowed to be at room temperature for at least 5 to 10 minutes before injection. Specimens were occasionally found to be toxic. They killed the animals. The toxicity is usually associated with severe nephritis, diabetes, and toxæmias of pregnancy. Such samples were detoxicated by treating with ether (3 c.cm. of ether for each c.cm. of urine). Ether removes all the toxic substances along with the aestrin present in the urine of pregnant women. Certain drugs such as ergot, quinine, eodine, luminol, aspirin, mercurio-chrome, when extracted in urine, prove toxic to the test animals. On receipt of a sample, the reaction and the specific gravity were noted along with other clinical data supplied. For the 24 hours' modification of Kelso, two white female rats of the necessary age were injected subcutaneously on the dorsum with one c.cm. of urine three times in a day at intervals of three hours. When the specific gravity of the urine was below 1010, the amount injected in both the rats was doubled.

Twenty hours after the first injection, both the rats were killed and their ovaries were examined naked eye for gross changes. In noting the results, attention was paid only to the ovaries; the uterus and the tubes were ignored. The reaction was deemed positive when both the ovaries were enlarged and hyperæmic. Haemorrhagic follicles were occasionally present, but they only indicated strongly positive reactions and were never present unless the ovaries were enlarged and hyperæmic.

A negative result is indicated by small, pale ovaries. It is important to note that both ovaries of each rat must show both enlargement and hyperæmia, for the reaction to be considered as positive. Either change alone is insufficient for a positive diagnosis.

#### *Results*

Two hundred samples of urine were tested concurrently in rabbits and rats as test animals for the diagnosis of pregnancy. Complete agreement was recorded in 195 samples. With the remaining 5 samples, the Friedman test and the 24-hour rat modification gave anomalous results. Out of 195 samples, 80 samples were found to be positive, suggesting the diagnosis of pregnancy, while the rest, being negative, excluded such diagnosis. Most of the samples were received from the Cama Hospital, and the results of 50 per cent of positive and negative tests were further corroborated by the clinical history and the subsequent follow up of the patients.

During the course of these investigations, a few samples of urine proved toxic and killed the experimental animals. The total number of such samples was ten, of which two were repeat samples. These eight cases included four cases of vesicular mole and one of albuminuria. A urine sample from one case showed heavy bacterial contamination. In the remaining cases, the cause of death in the experimental animals remained unascertained. Of ten samples of toxic

urine, four proved toxic to rabbits only and two to rats only. The remaining four samples were toxic to both rabbits and rats.

### Discussion

My experience with this test is limited to a series of 200 cases, nearly 50 per cent of which have been checked by subsequent clinical history. Tests were desired in these cases for the following varied reasons:—

(1) To detect products of conception, either in early pregnancy, threatened or suspected abortion, ectopic gestation, vesicular mole or chorion-epithelioma.

(2) To detect the presence of retained living chorionic tissue in biological contact with the uterus.

(3) To exclude pregnancy in cases of menorrhagia or amenorrhœa with a vague history suggestive of pregnancy.

(4) To exclude pregnancy in cases with a mass in the pelvis with a vague clinical history.

The test under consideration, while showing perfect correlation with the Friedman test, not only confirmed the diagnosis of pregnancy but excluded a large number of other pelvic conditions that stimulate pregnancy. The accuracy of the Aschheim-Zondek and Friedman tests has been shown to be almost identical. Both of these give accurate results in 98 per cent of cases. Richard Kelso in his series of 130 specimens came across five cases in which 24- and 72-hour results in rats showed disagreement. In all these five cases, the 24-hour rat test was positive while the 72-hour rat test was negative. Clinically, these cases did not turn out to be pregnancy. They were cases of tubo-ovarian abscesses receiving large amounts of some endocrine product for the treatment of sterility. In my series, only five samples tested by the two methods showed disagreement. Out of five samples, the Friedman test was positive four times and negative only once. The results of the rat tests in these cases were, though not frankly negative, quite indefinite. The cause of such a discrepancy was traced either to improperly selected animals, such as undersized and unhealthy rats, or to the very dilute samples of urine (specific gravity lower than 1010) that was injected into them. In one sample, when the Friedman test was negative, the two rats used for the test showed contradictory results, one showing positive and the other giving negative results. It was found that the rat which gave a strongly positive reaction was more than forty days old, giving obviously a false positive result. On the whole, false positive results in rats were very rare.

Considering the above results, the immature female rat compares very favourably with the rabbit or the mouse as an experimental animal. It stands toxicity better than immature mice. Aschheim and Zondek quote 17 per cent mortality in immature mice and only 3.5 per cent in immature rats. In my series, the mortality in rats was found to be about 4 per cent.

With this 24-hour rat test (Kelso modification), the results were obtained in 24 hours without loss of accuracy. The rapid reading of the result in 24 hours enhanced its value particularly in the diagnosis of ectopic gestation.

The Friedman test has certain advantages, but it has several disadvantages, such as the high cost of the rabbit, its difficulty of breeding and accommodation and isolation for a period of thirty days before use. Intravenous injections in the marginal ear vein require some skill. Moreover, some rabbits are known to be refractory. Goldberger and others (1934) in a series of 1,093 tests recorded 3.4 per cent of rabbits as refractory. With the death of a single rabbit used in the test, due to toxicity of sample or some other cause, the test has to be done all over again.

Similarly, the original Aschheim-Zondek test has certain disadvantages; mice being very small and delicate, their ovaries are very small, making it difficult to read the result. The results are read only after 96 hours. The natural mortality rate and that due to injections are quite high.

By adopting an immature female white rat as the experimental animal, the test becomes quite accurate, rapid, convenient and economic. Although the 24-hour rat test using two rats compared very favourably with the Friedman test in the rabbit, as is evident from the above investigation, whenever the test is done using rats alone, it seems advisable to follow the technique recommended by Richard Kelso using four rats for each sample, two rats being used for the 24-hour test and two others for the 72-hour test.

### Summary

(1) Two hundred samples of urine were subjected to the Friedman test and to the Kelso modification 24-hour rat test, with the variation that the 72-hour rat test was omitted. One hundred and ninety-five samples gave identical results by both the methods. In only five samples were the results found to be anomalous.

(2) In 50 per cent of 200 samples, the results obtained by the Friedman test and 24-hour rat test, Kelso modification, were confirmed by the history of the cases and their subsequent clinical termination.

(3) The immature female rat was found to be a suitable experimental animal, and with it the test was found to be quite accurate, rapid, convenient and economic; it could be suitably employed to replace the Friedman test or to supplement it whenever necessary.

The author wishes to thank Dr. J. Jhirad, Medical Officer of Cama and Albless Hospitals in Bombay, for supplying the material for investigation, including the clinical history of the cases and their subsequent follow up results.

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## A CASE OF ACUTE ENCEPHALITIS

By E. BUDZISLAWSKI, M.D.

Calcutta

(WITH A NOTE BY J. LOWE, M.D.)

THE patient, a young European male, arrived in Bombay in May 1943 from Egypt. During the last few days on board the ship he had felt unwell and on the day of arrival in Bombay he felt feverish and suffered severe pains in the head, body and limbs. In spite of considerable disability he took the train to Calcutta on the same day. He noticed difficulty in instability 'as though I was drunk' on standing on the train. He first attributed this to the motion of the train, but later he realized that it was caused by his illness. Of the later phases of the journey from Bombay to Calcutta he remembers little. He noticed that his vision was double for a day and that his hands were shaky and clumsy. He found it difficult to manage food. He slept little at night. On his arrival in Calcutta he was carried from the train and was put to bed where I was called to see him on the next day.

He still had some fever and was suffering from severe hiccup which made it very difficult for him to eat or drink. Examination revealed the following findings. Signs were confined to the nervous system. There was drooping of the right corner of the mouth; the right side of the tongue was flat and the tongue deviated to the right. The pupils were moderate in size but the right one was not completely circular; the reaction to light was present but slow, and convergence and accommodation were not perfect. Speech was very slow and indistinct, apparently due to the muscular affection of the tongue.

The third, fourth, sixth and seventh cranial nerves showed no abnormality.

All reflexes in the body were present and equal on both sides. There were no pyramidal symptoms. The muscular power of the left arm and leg was definitely reduced compared with that of the right side.

The patient answered questions but with obvious difficulty—difficulty in concentration and difficulty in speech. The superficial sensation and deep sensation were normal.

Micturition was normal; there was constipation. Examination of the thorax and abdomen revealed nothing.

The patient was unable to rise from the bed. There was much weakness and some inco-ordination.

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On the next day, examination of red and white cell counts, etc., showed nothing abnormal and examination of the fundus of the eyes also revealed no abnormality.

The patient was admitted into a hospital, and I did not see him again till his discharge eight days later. Unfortunately no examination of the cerebro-spinal fluid was made while he was in hospital. The fever had gone and he felt better; the speech was improved, the tongue was level but with a little deviation to the right. The hiccup had disappeared and also the drooping of the mouth. The patient was still weak but movements were carried out with a little difficulty. All reflexes were present and normal. Attempts to walk, however, were made with great difficulty and the gait was definitely staggering, though Romberg's sign was not definitely present.

The patient's mental condition was clear but there was a certain dullness and morosity which, his friends said, was very different from his normal friendly cheerful disposition. He still slept little at night and was drowsy in the day. Muscular power on the left side was still less than on the right.

At this stage I decided that this was a mild case of encephalitis and this diagnosis was later accepted by other physicians who examined the patient.

A few days later the patient went away to the hills and I saw him again six weeks later. The improvement was marked and his behaviour appeared almost normal. He walked fairly well but with a slight tendency to staggering. (His companion in the hills stated that his muscular control in walking up and down hills was still rather defective.) His movements were quite brisk and definite.

The pupils were of equal size, the right was not completely round. They reacted to accommodation but only slowly to light.

There was some wasting of the left forearm which measured  $\frac{3}{4}$  inch less than the right. It is doubtful if this difference can be explained by the greater use of the right arm. The tendon reflexes on the left side appeared slightly brisker than on the right. There were no other changes detectable anywhere.

Later the patient left Calcutta for England where he is now under the observation of a neurologist as a convalescent case of acute encephalitis.

## Discussion

The diagnosis of acute encephalitis was made in this case on the basis of my previous experience of the disease in Europe and on my knowledge of the literature of the subject. The hiccup is a very characteristic sign, as also are the inversion of sleep (restlessness at night and drowsiness during the day), the ocular symptoms, the onset, the course and the fleeting nature of some of the nervous symptoms. The absence of meningeal bulbar and spinal symptoms also points to acute encephalitis. Severe rheumatic



pains (as observed in our case) are seen in many varied conditions, but seen in connection with paralytic or paretic signs, and followed by trophic changes in certain muscle groups, they may be of diagnostic value in the absence of any other explanation.

Since it appears doubtful if any such cases have previously been recorded in India, I am publishing this note on this case.

*Note by J. Lowe, M.D.*

The case described above was seen by me and the diagnosis was accepted. My experience of this condition is very limited, a few cases having been seen by me in England, twenty years ago. I propose here merely to discuss some broad outlines of the disease and its possible occurrence in India.

The disease is considered to be a virus infection of the central nervous system, although nothing precise is known of its causative organism. Twenty years ago there was an epidemic of this disease in Europe but for the last ten years in Europe it has been rare, although the annual recorded deaths attributed to this cause in England and Wales have been persistently over 600. The accuracy of the diagnosis of some of these cases is open to question.

All authorities, however, agree that post-encephalitic Parkinsonism (so called because of its resemblance to paralysis agitans or Parkinson's disease) has been frequent in Europe including Great Britain up to the present time; this fact indicates that the disease is still present. Authorities also agree that many cases of acute encephalitis are exceedingly mild, but also that the mild cases are almost if not quite as frequently followed by the development of Parkinsonism as are the severe cases. A patient not infrequently suffers from a mild febrile attack with possibly some vague nervous symptoms, and it is only later when Parkinsonism develops that the true nature of this febrile attack is realized. Authorities such as Walshe state that Parkinsonism occurs in something like 50 per cent of cases, even mild ones.

The severity and the clinical course of the illness varies in the widest possible manner; some cases may be very mild such as the one described above, and the patient may be ambulant. At the other extreme we have a very severe febrile illness lasting only a short time, with symptoms indicating marked nervous involvement. Some cases may show violent delirium and involuntary movements, either like chorea or of the 'myoclonic' type causing jerking or twitching.

The development of Parkinsonism is described by Walshe as follows:—

'Either during the phase of convalescence, or two or three years later, the slow development of the Parkinsonian syndrome occurs in over 50 per cent of cases. Gradually and very insidiously an extrapyramidal type of muscular rigidity invades the musculature, producing the Parkinsonian mask, the slow

and restricted movements, and occasionally the tremor of paralysis agitans. This state may at first be confined to a single limb, spreading later to the others and becoming generalized. It runs a progressive course and finally, after a variable period of years, disables the sufferer, who becomes emaciated and finally succumbs. In a very few cases it undergoes arrest at some stage short of grave disability.

The early stage of this condition is commonly undiagnosed, for the syndrome is made up of such slight deviations from the normal that, unless the general inspection of the patient as he moves and performs his natural actions reveals the typical slowness and limitation of range of movement, routine examination may fail to detect the disorder. Perhaps the earliest symptom is a failure of an affected arm to swing as the patient walks. If it be the right arm that is affected, the handwriting becomes slow and laboured, and the script progressively smaller as the months go by. The gait becomes slow and gliding in character, the figure slightly bowed and the face fixed. Close examination will reveal a fine flutter of the closed eyelids, a defect of convergence, a "cogwheel" rigidity of the limb musculature, or less commonly a visible tremor. The patient salivates freely by night, if not also by day.

In the initial phase, the patient's complaints are apt to seem out of proportion to anything that examination reveals, and many of the sufferers labour for many months or even longer under a diagnosis of "neurasthenia". If the condition develops unilaterally, a progressive hemiplegia may be diagnosed and an intracranial neoplasm suspected. Yet despite all this, once the syndrome has been seen and duly noted, it should never fail to be recognized.

One other common, though not invariable, feature of post-encephalitic Parkinsonism may be mentioned. It goes by the name of *oculogyric crisis*, and consists of a forced upward deviation of the eyes, with head retraction, lasting for from thirty minutes to an hour and causing some distress.

In children another post-encephalitic sequel is mental and moral deterioration, leading to refractoriness and sometimes to delinquency.

The question arises as to whether this disease has been found and is found now in India. The present case must be regarded as imported. I have never seen a case in India, but various professional colleagues have given information indicating that such cases do occur. Dr. R. N. Chaudhuri states that he has during the last few years seen several cases of typical Parkinsonism occurring after an illness of doubtful nature. A few months ago he saw a typical case of oculo-gyric crisis. Colonel G. Taylor, Consultant Physician, Eastern Army, and late Professor of Medicine, Medical College, Lahore, states that he saw some cases before the war in the Mayo Hospital, Lahore, and that it was often confused with other cerebral conditions, but the diagnosis was confirmed (in some cases) by the subsequent development of Parkinsonism. In the out-patient department at Lahore, cases of Parkinsonism were seen. One or two other hospital reports indicated the occurrence of an occasional case of acute encephalitis.

There is therefore considerable evidence that cases of acute encephalitis do occur from time to time in India and it is not impossible that this war, as did the last, may bring an epidemic of this condition. It is therefore felt that the publication of this case and discussion may be of interest.

# HIGHLY POTENT WHOLE LIVER EXTRACT

HG % RBC count

100	5
90	4.5
80	4
70	3.5
60	
50	
40	
30	



2cc. 2cc. 2cc. 2cc. 2cc.



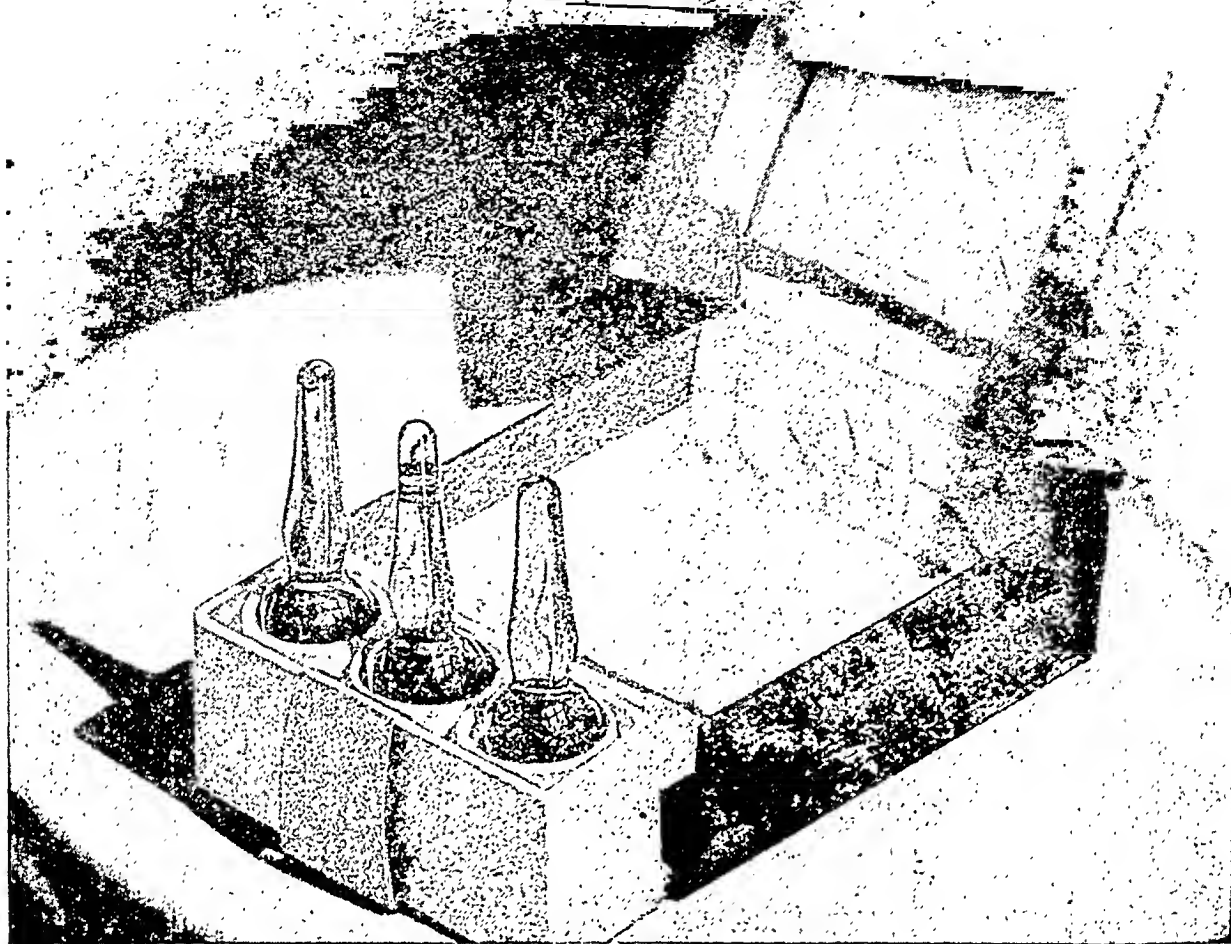
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# Indian Medical Gazette

FEBRUARY

## THE DIAGNOSIS OF MALARIA, AND FIELD'S RAPID METHOD OF STAINING PARASITES IN BLOOD FILMS

EVEN in normal times when adequate quinine is available, the common practice of giving quinine to all patients complaining of 'fever' is to be considered bad medicine, for only a fraction of these patients have malaria and need quinine. In the present shortage of quinine, such a practice is to be utterly condemned as involving a tragic waste of quinine.

While thorough clinical examination, including a careful history, will usually give a strong indication whether or not the patient with 'fever' has malaria, with modern methods of staining blood films it often takes less time, gives less trouble, and is always much more satisfactory to base diagnosis on examination of blood films. This should always be done when possible.

Some hospitals in India are adopting the policy that quinine can be given only to patients in whose blood parasites have been demonstrated, and this policy has not only affected a great economy in quinine (up to 75 per cent in one hospital), but also has made for greater efficacy of treatment of malaria, for those who show parasites are then treated properly and not half-heartedly.

The making and staining of blood films and the easy demonstration of malaria parasites in them have been greatly facilitated by the methods of Field. By these methods it is possible for one worker with an assistant to make, stain, and examine up to thirty or even forty films within an hour. In dealing with an individual patient, the blood film can be taken, can dry, be stained and examined within ten minutes. The actual staining is complete in ten seconds. Other rapid, cheap and widely applicable methods of staining blood films have been described by various workers. One such method was described by Simeons in this Journal (Vol. 77, December 1942, p. 725).

With such methods available, there is no excuse for the doctor who has a microscope but who makes no attempt to demonstrate malaria parasites.

Field's stain is quite easy to make; the ingredients are available in India; the stain keeps well and is very economical in use.

*The making of the blood film.*—The slide used should be clean. The blood is taken by pricking

the patient's finger or ear lobe (the skin having previously been cleaned with spirit and allowed to dry) and one smallish drop of blood is placed on the slide slightly nearer one end of the slide than the other. With the needle used for pricking the skin, the blood is spread in the form of a circle; about the size of a one anna piece is usually about right. The film (which is quite thin) dries rapidly, and, when dry, it should be possible to see the hands of a watch through it.

*The staining and examination of the blood film.*—The methods of making Field's stain were described by Field as follows:—

*'Preparation of stain.*—Two solutions are used—methylene blue-azure and eosin, both isotonic solution adjusted to pH 6.6. Isotonicity and correct pH are determined by the amount and proportions of the acid and alkaline phosphates which the stains contain.

### Solution (A).

Methylene blue*	..	..	0.8 gramme
Azure I†	..	..	0.5 ..
Disodium hydrogen phosphate (anhydrous).			5.0 grammes
Potassium dihydrogen phosphate (anhydrous).			6.25 ..
Distilled water	..	..	500 c.cm.

### Solution (B).

Eosin*	..	..	1.0 gramme
Disodium hydrogen phosphate (anhydrous).			5.0 grammes
Potassium dihydrogen phosphate (anhydrous).			6.25 ..
Distilled water	..	..	500 c.cm.

\* Medicinal methylene blue and azure I: 'Supplied by G. T. Gurr of London.

Yellow eosin, water soluble: Supplied by British Drug Houses, London.

† The American equivalent of the German azure I is azure B, not as has been sometimes wrongly supposed, azure A.

The phosphate salts are first dissolved, then the stain is added. Solution of the granular azure I is aided by grinding in a mortar with a small quantity of the phosphate solvent. The solutions of stain should be set aside for 24 hours when, after filtration, they are ready for use. Should a seum later appear on the surface, or dye precipitate on the stained films, subsequent filtration is necessary.

The same solution may be used continuously for many weeks without apparent deterioration but the eosin solution should be renewed when it becomes greenish from the slight carry-over of the methylene blue.

The stains are kept in covered jars of such a size that the depth of solution is about two inches, the level being maintained by the addition of fresh stain as necessary.

Should azure I be unobtainable it is possible to prepare a methylene blue-azure mixture of undefined composition from medicinal methylene blue. A simple method of producing a satisfactory solution, solution (A), from methylene blue and buffer phosphate salts is as follows:—

(i) Dissolve 1.3 grammes of medicinal methylene blue and 5.0 grammes of anhydrous disodium hydrogen phosphate ( $\text{Na}_2\text{KPO}_4$ ) in 50 c.cm. of distilled water.

(ii) Bring to the boil and then evaporate in a water bath almost to dryness.

- (iii) Add 6.25 grammes of anhydrous potassium dihydrogen phosphate ( $\text{KH}_2\text{PO}_4$ ).
- (iv) Add 500 c.cm. of distilled water, stir till the stain is completely dissolved and set aside for 24 hours.

(v) Filter before use.

[Copied from FIELD (1941). *Trans. Roy. Soc. Trop. Med. Hyg.*, 35, 35.]

The dried blood film is dipped for about two seconds in solution A, then washed for two or three seconds by gentle motion in a jar of ordinary water, then dipped for one second in solution B, immediately washed again in water for a second or two, and then allowed to dry, which takes only a few minutes.

With various lots of stain, the staining times may need to be varied a little. More time is needed in solution A than in solution B.

In a properly stained film, the red cells hardly show at all, the leucocytes including their granules are well stained, the blood platelets are stained pinkish blue, and the malaria parasites are well seen, with red chromatin, blue protoplasm, and, in the maturer forms, hæmoglobin pigment. The red cell containing the parasite is frequently invisible, although sometimes it can be seen faintly and Schuffner's dots may also be seen. Both sexual and asexual forms of the parasite show well.

Very minute forms of *P. falciparum* may be a little difficult to spot, but if present they are usually numerous.

No film should be reported positive merely on the finding of one or two 'doubtful' parasites. Parasites if present are usually present in fair numbers, and can almost always be detected within one minute. Prolonged search is usually not necessary.

By the general use of the rapid method of staining described, the accuracy of diagnosis of malaria can with very little trouble be greatly increased.

With the use of this method it is possible to adopt a policy of giving quinine only to those patients showing parasites, and the waste of quinine can be very greatly reduced; while those patients who have malaria can be properly treated.

Fifteen grains of quinine a day for seven days is usually enough to control an attack well, though some relapses will occur, as with any form of treatment. With infection with *P. falciparum* it may be advisable to give more quinine for the first forty-eight hours.

J. L.

## PROTEIN HYDROLYSATES IN SHOCK AND INANITION

THE idea of the use of protein hydrolysates in conditions of hypoproteinæmia is not a new one; they were first used experimentally in starved animals thirty years ago. Recently, however, various writers have discussed the possibility of their intravenous administrations in human beings, and the conditions which seem to call for such medication are shock, hypoproteinæmia and inanition.

A certain amount of work has been done on this subject, but on a very limited scale, and mainly in America. Difficulty has been experienced in producing a hydrolysate which did not give rise to allergic or other reactions.

Work on this subject has been going on for some time in the Institute of Hygiene, Calcutta, under Dr. K. V. Krishnan, and when the famine conditions recently developed in Bengal, the work was accelerated, suitable protein hydrolysates were prepared by a modified method, and these have been widely used in the treatment of inanition caused by starvation.

An account of this work has reached us too late for publication in the present issue, and it will be published in our next issue.

## Special Article

### TREATMENT AND MANAGEMENT OF STARVING SICK DESTITUTES

PREPARED BY THE COMMITTEE OF ENQUIRY INTO EFFECTS OF STARVATION, INDIAN RESEARCH FUND ASSOCIATION

(From the All-India Institute of Hygiene and Public Health, Calcutta)

#### Introduction

THIS report is being written primarily at the request of the army and civil authorities who

are undertaking the organization of emergency hospitals and camps for dealing with 'sick destitutes' in Bengal. For these emergency hospitals special lists of drugs and requirements (*vide* Appendix I) have been prepared to cover the essential needs only, and the treatment outlined in the present notes is based in general on the items included in these lists.

This report is written on the basis of experience in Calcutta during the months of September, October and November 1943, when acute or

sub-acute starvation was widely seen, and it is possible that in the future in different circumstances the situation may be rather different and demand rather different measures. It is however felt that these notes should be of general value.

*Types of cases.*—One feature noted in Calcutta is the relative rarity of marked signs of vitamin deficiency. Frank cases of beri-beri, scurvy, etc., have not been seen. It seems, however, possible or probable that in more chronic starvation these vitamin deficiency diseases will be more common, and also that, unless the vitamin intake is adequate, the patients will develop these diseases during or after the treatment for sub-acute starvation.

The cases admitted to hospital from the 'sick destitutes' found on the streets of Calcutta could be divided roughly into three groups: (a) those suffering from inanition due to starvation only, (b) those suffering from inanition due to a combination of starvation and disease, and (c) those showing relatively little inanition but suffering from acute disease. The methods of handling and management of these groups of cases therefore differ somewhat.

*Diagnosis.*—The diagnosis of inanition is comparatively easy. The patient is usually very thin and weak and shows the characteristic mental picture of inanition, often a marked apathy. The skin is dry and cold, all the organs and tissues are shrunken, the subcutaneous fat is completely absent, the temperature is subnormal, systolic, diastolic and pulse pressures are reduced. The eyes are shrunken and there are frequently other signs of dehydration. Often the wasting of the limbs is masked by the presence of œdema. (Care should be taken to make sure that this is not caused by nephritis.) There is sometimes present a diarrhoea and colitis which may be neither bacillary nor amœbic.

The diagnosis in patients of the second group, those showing inanition plus disease, is often more difficult. The predominating clinical picture is that of inanition, and moreover the presence of disease may be completely masked by the inanition. The patients will frequently show malaria parasites in the blood, but have no temperature and show no splenic enlargement.

Similarly in the presence of an infection which commonly causes high fever, the temperature may be subnormal, apparently as the result of inanition. In the same way, cases of amœbic dysentery may show little diarrhoea and stools not typical of the disease. Such patients are frequently admitted to hospital and treated for inanition, and when the general condition begins to improve they develop the fever and other symptoms which are characteristic of the infection from which they are also suffering.

The diagnosis in patients of the third group presents no particular feature. The patients,

though weak, are usually not collapsed, the pulse is good though often rapid, the body temperature is frequently raised, and the patients show the typical manifestations of the diseases from which they are suffering. The common diseases found have been malaria mostly malignant, dysentery sometimes amœbic but more often bacillary, pneumonia, nephritis, bronchitis, 'Naga sore', tuberculosis, anæmia, urinary tract infections, etc.

*Treatment, general.*—If the predominating clinical picture is that of disease, then the emphasis should be laid on treatment for that disease, but if, as is usual, the predominating clinical picture is that of inanition, then the inanition should be treated first. Many of the patients have been exposed to cold and have little or no clothing, and a good supply of clothing, blankets and bedding is essential. The treatment of inanition and of the diseases frequently found in these 'sick destitutes' is described below.

*Dosage of drugs.*—In considering the treatment of these patients it should be remembered that the body-weight of most of them is abnormally low, and also that they are usually very weak. The dosage of drugs therefore has to be planned accordingly. In general, the ordinary standard dosage of any drug should be halved, and this principle has been adopted throughout these notes.

*Treatment, dietetic.*—Diet treatment in disease superimposed on starvation is important. A healthy person suffering from acute infection may require little diet during treatment, since he has adequate reserves. A starved person suffering from acute infection has no reserves, and the diet must be kept at the maximum possible level. Only in inanition and severe gastro-intestinal disorders should the diet be markedly restricted and then only for the minimum possible time. A highly nutritious fluid diet is of vital importance in this work.

### *Inanition*

A considerable number of patients may be brought to hospital in a state of collapse.

*Treatment of collapse.*—The general treatment for collapse should be adopted—rest, warmth, warm fluids, etc., followed by a suitable diet, but in severe cases intravenous therapy is strongly indicated and special preparations of protein hydrolysates containing vitamin B complex with glucose are being made available. If this is not available, or is contraindicated, 5 per cent glucose saline may be given.

*Intravenous peptone glucose.*—Intravenous injections of peptone glucose are recommended for all advanced cases of starvation in a state of collapse. (Cases of group I and sometimes of group II *vide infra*.) The injections help to revive the cases quickly and enable them to take suitable diet by the mouth.



Peptone glucose for injection is supplied in screw-capped transfusion bottles. It is a mixture of 5 per cent glucose, 5 per cent protein hydrolysates and contains riboflavin, nicotinic acid and thiamin. It is of a clear port-wine colour, free from precipitate or turbidity. Every batch before issue is tested bacteriologically for sterility, immunologically for freedom from allergic reactions, and pharmacologically for absence of toxicity.

The quantity contained in each bottle is usually 200 c.cm., which represents the average dose for one injection for an adult. Bottles containing 400 c.cm. are also supplied.

The bottles are best stored in the dark in a cupboard at room temperature. Storage tends to deepen the colour but this is of no consequence. Bottles showing precipitate or turbidity or giving out a foul odour on opening should be rejected. On opening the screw caps of good bottles, a noise is heard due to the rushing of air into the vacuumized bottles; when the caps are found loose, it is best to reject the bottles. Once the cap is opened, the material must be injected within 2 hours, as otherwise bacterial contamination and growth will occur.

**Selection of cases.**—Before giving injection to a patient, it is advisable to examine the urine for albumin and casts, but this is not absolutely essential. Even where no urine is available or where the patient is in an extreme state of collapse or the urine shows traces of albumin (as most cases of advanced starvation do), peptone glucose may be safely administered. But if there is general oedema, and if kidney and liver damage is suspected, it will probably be advisable to adopt other methods of treatment.

Nutritional oedema cases may improve markedly after peptone-glucose injection.

**Technique.**—The intravenous injections are best given with the help of Haye's pattern transfusion set (figure 1). The screw cap of the bottle is removed and the cork of the transfusion set (previously washed and sterilized) fitted on to the bottle. The bottle is inverted and hung up, and the clamps on the rubber tubing adjusted till the fluid comes out in drops (60 per minute) from the needle. The latter is then introduced into the vein and the fluid allowed to go in slowly. An injection of 200 c.cm. should take an hour to administer. Rapid administration may not be tolerated well. 400 c.cm. is the maximum daily dose. It may be given in one dose or preferably in two doses of 200 c.cm. each, one in the morning and the other in the evening. The effect is often immediate and lasts about 24 hours. The cases generally need as many as three injections on 3 consecutive days. A total of 600 to 1,000 c.cm. in 3 days often results in marked improvement and should be supplemented by nasal feeding (*vide infra*) or by hospital diet by mouth as indicated. It is essential to remember that one injection provides only about 100 to 200 calories, and therefore as the patient improves it should be supplemented

by proper diet. So far there has not been any necessity for giving injections for more than 3 days, but if required they may be continued for another 3 days with benefit.

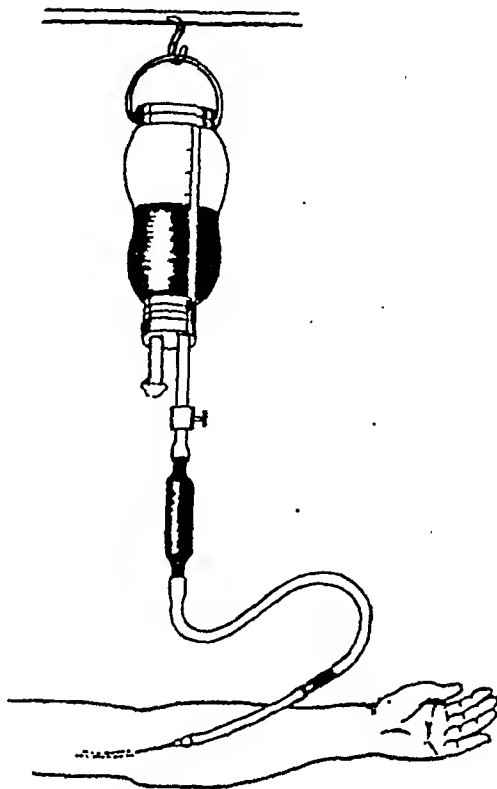


Fig. 1.—Haye's pattern intravenous transfusion technique.

**Reactions.**—In none of the cases so far injected has any adverse reaction been noted.\* Improvement in the pulse, respiration, blood pressure and general condition usually follow the injection. In a few cases a latent malarial infection has flared up after one or more injections and prompt treatment with anti-malarial drugs has cured the disease.

**Cleaning and sterilization.**—After using the transfusion set, it should be immediately washed thoroughly in clean water and resterilized for use. This is important, as otherwise the fluid in the set may decompose with the formation of toxic substances which if not properly washed may give rise to untoward results.

#### Dietetic treatment

**Selection of cases.**—To simplify dietetic treatment, cases may be roughly categorized on admission as follows:—

**Group I.**—Collapsed cases, likely to die without parenteral feeding and therapy. These may be oedematous or severely dehydrated and are in the last stages of acute or chronic starvation. They are incapable of taking even simple liquid diet by ordinary methods of feeding, as they are usually semi-comatose.

\*In a few more recent cases, mild reactions have been seen.—Editor.

*Group II.*—Less markedly collapsed cases, capable of recovery ordinarily by oral feeding. Anorexia and even failure of thirst may be present, so that individual spoon feeding may be necessary. Semi-solids and even milk may not be retained in the first day or two after admission.

*Group III.*—Cases capable of taking simple milk diet.

*Group IV.*—Cases usually capable of obtaining nourishment from a good gruel and likely to be able to look after themselves after a few days in hospital.

*Treatment.*—Treatment of group I patients by intravenous peptone glucose has already been discussed (*vide supra*). This should be supplemented by appropriate diet. Where necessary nasal feeding may be resorted to.

*Nasal feeding.*—In the treatment of cases of group II (and also in cases of group I during the phase of recovery) the administration of small amounts of food at very short intervals is needed. The following note describes one method of feeding such patients.

The apparatus used is the same as that for peptone glucose. A Ryle's tube is passed into

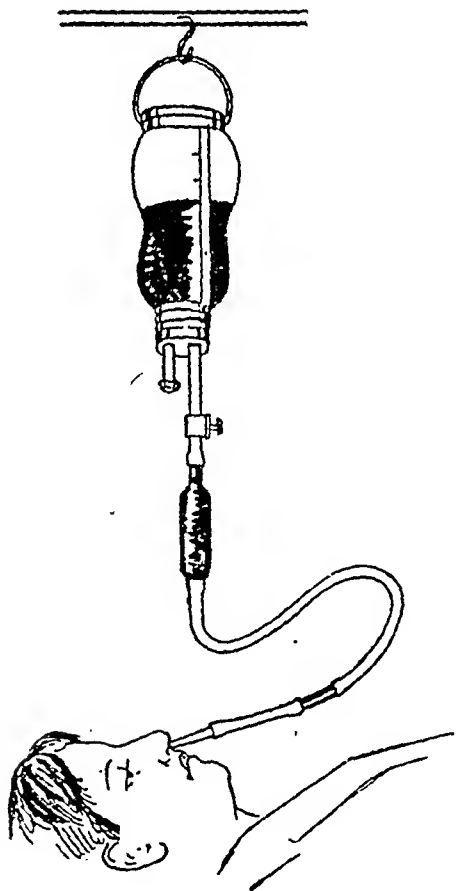


Fig. 2.—Nasal feeding through Ryle's tube.

A suitable fluid for administration is as follows:—

	Calories	Protein grammes
Milk (skimmed or ghol), 4 pints	800	80
Glucose, 4 oz. .. ..	450	..
Salt, 1 oz. .. ..	..	..
Eggs, 2 .. ..	+ 120	10
Shark liver oil, 1 oz. ..	50	..
Compound vitamin tablet, 1	..	..
	1,420	90

Up to 4 pints can be given in a day which contains about 1,500 calories with 90 grammes protein and large quantities of all vitamins.

If liver is needed, 2 to 4 ounces of liver is pulped and sieved through muslin. One to 2 ounces of this pulp can be run down the stomach-tube twice daily, after disconnecting it temporarily from the drip apparatus, this adds a further 160 to 320 calories. The stomach-tube should be taken out and boiled every day when liver is administered.

*Hospital diets.*—A series of hospital diets roughly corresponding to the needs of cases in groups II, III and IV is given below. Each case may be put on the appropriate scale on admission and upgraded according to progress. The need for administering vitamin concentrates from the early stages is stressed.

It is evident that a somewhat crude and incomplete programme of hospital treatment will be necessary, if the small number of beds available is to be used to best advantage.

Cases in hospital should be upgraded as rapidly as progress permits in order that beds may be freed.

For simplicity in dietetic treatment, the hospital kitchen should prepare stocks of the various food mixtures according to the recipes given below, in quantities corresponding to the numbers of patients in each category. The medical officer could keep a card with each patient, stating his clinical group (changed according to progress) and the amounts of each mixture to be fed daily (adjusted in accordance with age and clinical condition). The work of actual feeding could thus be reduced to a drill. Calorie values for the standard diets and for half-pint quantities of the standard food mixtures are given to simplify caloric control. Adult patients should receive no less calories daily than those provided in each standard diet. Children should receive smaller portions in proportion to their size.

*Ration scale.*—The following ration scales are suggested as a basis for the bulk provision of food. They are designed for a unit of 10 'average' patients (including women and children) being fed daily. Provisionally it may be assumed that equal numbers of patients will require each type of diet.

the stomach by the nasal route attached to the adapter of the infusion apparatus and left in the stomach.

Corresponding to clinical group	DAILY SCALES OF HOSPITAL RATIONS PER 10 PATIENTS					
	Fluid diet II		Milk diet III		Gruel diet IV	
	lb.	oz.	lb.	oz.	lb.	oz.
Flour (barley, rice or maida)	2	8	1	4	..	..
Sugar ..	2	8	2	8	2	8
Milk, fresh (tinned, dried or ghol) (a) ..	..	..	20	..	10	..
Cereal mixture (b) ..	..	..	..	..	6	..
Dhal ..	..	..	..	..	1	8
Vegetables (c) ..	..	..	..	..	2	8
Salt ..	..	5	..	5	..	5
Condiments ..	..	..	..	..	..	1
Compound vitamin tablets ..	(No)	10	(No)	10	(No)	10
Shark liver oil ..	..	$\frac{1}{2}$	..	$\frac{1}{2}$	..	$\frac{1}{2}$
Calories per head (approx.) ..	800		1,200		1,900	

Extras (per 10 patients).

(Admissible on demand, in addition to above diets if available.)

- |                            |                              |
|----------------------------|------------------------------|
| 1. Yeast .. 5 oz.          | 6. Non-citrous fruits 1 lb.  |
| 2. Liver .. 1 lb.          | 7. Fresh fish .. 1 lb.       |
| 3. Onions .. 5 oz.         | 8. Glucose .. 1 lb.          |
| 4. Buttermilk (a) .. 8 oz. | 9. Compound vitamin tablets. |
| 5. Citrous fruits .. 10    | 10. Shark liver oil.         |

Notes.—(a) Buttermilk (ghol) is intended for use as a 'starter' for making curd, etc., from ordinary milk.

(b) Cereal mixture should contain not less than 50 per cent rice, the balance being made up from atta or maida flour as available. Millets should not be used in a hospital dietary.

(c) Vegetables should include 50 per cent green vegetables.

**Standard recipes.**—The following recipes give quantities for 10 average patients.

(a) *Fluid diet, conjee.*—Make  $2\frac{1}{2}$  pounds flour into a paste with water, and add water to make up 3 gallons. Bring to the boil and cook until a thin gruel is produced. When cool, add  $2\frac{1}{2}$  pounds sugar and 5 ounces salt and stir in. Shark liver oil  $2\frac{1}{2}$  and yeast 5 ounces may be added (approximate calorie value—150 per half pint).

*Fruit drink.*—If materials are available, make a drink from fruit juices, sugar (or glucose) and water.

(b) *Milk diet, conjee.*—May be prepared as above.

*Milk.*—If not tolerated, dilute with water as necessary. Two ounces of sugar should be added to each seer of milk. (Approximate calorie value of sweetened *undiluted* fresh milk or canned or dried milk diluted to fresh milk equivalence—220 per half pint.)

*Ghol.*—A portion of the milk available may be used to make 'ghol'. To each gallon of slightly warm fresh or diluted tinned or dried milk add 4 ounces of prepared buttermilk (*vide* extras no. 4). Stir and allow to stand overnight in a warm place. Next day churn up the curdled

mass. (Approximate calorie value—200 per half pint.)

(c) *Gruel diet, gruel.*—Put  $1\frac{1}{2}$  pounds of dhal into a large vessel, and add  $1\frac{1}{2}$  pints of water and boil till soft. Then add 1 gallon of water and 6 pounds of cereal mixture. Again bring to boil. When the cereal is half cooked, add  $2\frac{1}{2}$  pounds of chopped vegetables and continue cooking till cereal is fully cooked. Remove from the fire and add 5 ounces of salt and 1 ounce of condiments, and stir in. (If onions are available they may be added with the vegetables. Sugar may also be added, according to the taste of patients.) Approximate caloric value—340 per half pint.

**Preparation and serving.**—The above food preparations may be prepared in bulk in the kitchen according to the numbers of patients on each type of diet. The medical officer should note on each patient's card how much of each mixture should be given, and at what intervals. He can easily estimate the number of calories being provided from the figures in the preceding paragraph. It may be noted that the *calorie value of the average fluid and milk diet is too small to support life indefinitely*. These two diets should therefore be considered as interim treatment designed to carry over the patient until fit to consume the gruel diet.

The actual portion of each food given to patients should be prescribed by the medical officer in accordance with the age and condition of each. The calorie intake should therefore be higher than 'average' for adults, and lower for children.

The importance in many cases of small frequent feeds has already been stressed,

### Malaria

As already stated inanition may mask malarial infection, and the signs of malarial infection may not be present on admission, but fever, etc., may develop later. In areas in which malaria is highly endemic and in the malaria season, malaria may be so common as to justify *mass treatment* of all patients, but in other areas and even in highly endemic areas outside the malaria season, this will not be justified. In view of the shortage of quinine, accurate diagnosis of malaria is highly desirable and, if available, microscopic examination of blood films should be used. (Field's method of rapid staining is very useful in such circumstances, *vide* appendix II.\*) Clinical diagnosis can be fairly accurate with experienced workers.

Malaria in starved or semi-starved persons is readily treated by ordinary methods, the dosage being regulated according to body-weights; *generally 15 grains, and not more than 20 grains, of quinine should be given in a day and treatment should be given for 7 days. Oral administration is usually effective.* For this purpose quinine sulphate (or cinchona febrifuge) is recommended.

In severe cases with vomiting or cerebral symptoms, intravenous injections are recommended but they should be given with great care. Not more than 5 grains should be injected and it should be dissolved in at least 20 c.cm. of distilled water and injection should take at least 10 minutes. Or preferably the quinine may be given in 200 c.cm. of glucose saline. Quinine bishydrochloride should be used for this purpose. As soon as possible, injections should be abandoned for oral administration.

It is not usually considered necessary to give quinine for more than 7 days. The routine use of pamaquine is not considered advisable. Atebrin or mepacrine in half the usual dosage may be used if quinine is not available. The full army course of malaria treatment, the 2, 5, 2, 5, treatment, is not considered necessary or advisable in these cases.

### Pneumonia

Cases of pneumonia should be treated with M&B 693, 2 tablets at once and 1 four-hourly till the temperature falls; a four-day course is usually sufficient. Adequate fluids must be given. (Pneumonia may develop during the phase of recovery from inanition.)

### Intestinal disorders

Acute purging, vomiting, etc., may be due to cholera, bacillary dysentery, or food poisoning. The more chronic diarrhoeas may be due to bacillary dysentery, amoebic dysentery, or to 'famine diarrhoea'. The fulminant dysenteric attack should be treated along the same lines as cholera, and therefore differential diagnosis is

unnecessary. Of the less acute conditions, bacillary dysentery is much more common than amoebic, and since microscopical examination will usually not be available, *dysenteries should be treated as bacillary unless there is a definite indication to the contrary* (e.g. absence of fever, character of stools, lack of response to the sulphonamides).

*Bacillary dysentery.*—This should be treated with sulphaguanidine, 3 grammes given at once and 1½ grammes given four-hourly; or by M&B 693, 2 tablets at once and 1 tablet four-hourly. Sulphaguanidine is less toxic but has no effect on the respiratory, urinary and other infections from which these patients are often suffering. M&B 693 is effective against all these, but is more toxic. An adequate intake of fluids is essential during its administration. Under either treatment the symptoms should abate within 24 to 48 hours and treatment for limited periods (4 days) is usually effective. If symptoms do not subside, the correctness of the diagnosis should be questioned.

*Amoebic dysentery.*—This should be treated with emetine, half-grain doses injected daily for 6 days. If the diagnosis is correct, diminution in symptoms should be observed by the third day.

*Nutritional diarrhoea.*—This is frequently seen and should be treated along dietetic lines.

*Cholera.*—Cholera cases should be isolated and treated along usual lines with the immediate rapid transfusion of up to 3 pints of hypertonic saline, followed if possible by slow drip feed, or repeated transfusions, of isotonic saline until the blood pressure shows a reasonable and maintained rise, and until the urine output average 6 ounces in 4 hours. If suppression of urine persists and signs of uræmia appear, hypotonic saline with alkalis should be given intravenously. As soon as possible a large intake of fluids by mouth should be established.

### Œdema

Œdema is commonly seen among sick destitutes. There are two main causes: (a) nutritional œdema, (b) nephritis commonly secondary to septic skin conditions particularly scabies, and exposure to cold. In the cold weather the second group may predominate.

It is important to distinguish between the two types since *in the second type intravenous injection of saline and protein hydrolysate is absolutely contraindicated.*

Nutritional œdema is less extensive, and less marked. Albumin in the urine if present is very small in amount, and there are no casts, red cells, etc. In such cases the *blood pressure may be low*, the heart is weak but normal in action.

In nephritis the œdema may be very extensive and marked general anasæra, ascites, etc., are common, the urine usually shows albumin casts, red cells, etc. (though these may very occasionally be low or even absent), and the

\* This information is given in our editorial (p. 73) and appendix II is omitted.—Editor.

blood pressure is not low, and in the acute cases seen here the heart has been normal. In similar cases reported elsewhere in Bengal cardiac complications have been reported.

In cases of nephritis, low diet, low-fluid intake, salt-free diet, etc., should be the treatment.

### Anæmia

Some degree of anæmia, usually macrocytic, has been seen in 80 per cent of Calcutta cases and in some cases it has been very severe. Directly and indirectly anæmia may contribute to the death rate.

All patients in hospital should get some form of animal protein, at least 2 or 3 times a week, and except in cases of diarrhoea or dysentery, ferrous sulphate in doses of 3 to 6 grains should be given to all persons. Yeast may also be added to the diet with great advantage.

In all patients showing marked anæmia, treatment should be promptly instituted. Liver should be given, by injection 2 to 4 c.cm. daily up to 6 days, and this course should be repeated after two weeks. If adequate supplies of injectable liver products are not available, 100 to 200 grammes of liver, powder, liquid or lightly cooked, should be given daily for 7 to 10 days to the less severe cases of anæmias.

Anæmia associated with malaria will usually respond well to treatment for malaria which should therefore be given first. Later, if necessary, the anæmia should be treated. In very severe anæmia with malaria, treatment for the two conditions should be given.

### Skin conditions

*Ulcers.*—Phagedenic ulcers, particularly 'Naga' sores, are very common in such patients. If untreated, the ulcers may extend deeply, affect bones and cause death. The general treatment consists of rest, good food and personal hygiene. The local treatment recommended is as follows:—

(a) The application twice a day of compresses consisting of saturated magnesium sulphate solution or a mixture of saturated magnesium sulphate and 1 in 2,500 potassium permanganate, equal parts. These applications are continued until the sloughs have separated.

(b) The ulcer is then dusted with boric powder containing 1 in 10 sulphanilamide powder. This dressing can, if necessary, be left for several days. The dressing is continued until the ulcer heals.

*Scabies.*—The patient is given a good wash with soap and warm water; the skin surface is scrubbed well with a hard brush or a rough towel; the wash is given preferably towards evening. The patient is then given a quantity of the ointment (unguentum sulphuris B.P. 1 dram to 1 ounce) sufficient to cover his whole body (about 3 ounces of ointment is required for one application for every adult); this he rubs in vigorously for 20 minutes to half an hour and then puts his clothes on and goes to bed.

This process is repeated for 3 consecutive nights and on the morning of the fifth day he gets a good bath and wears fresh clothes and the treatment is complete.

Any sores which are left after this treatment should have dilute ammoniated mercury ointment 1 per cent to apply daily.

### APPENDIX I

#### LIST OF DRUGS, ETC., ISSUED TO HOSPITALS 'Acute' hospitals

##### AMOUNTS FOR A FORTNIGHT

Drugs	20 bedded hospitals	50 bedded hospitals
1. Aspirin tablets 5 grains.	150 tablets	375 tablets
2. E.C. ..	2 bottles	5 bottles
3. Ferri sulph., 3-grain tablets.	200 tablets	500 tablets
4. Hypertonic saline tablets.		63 tablets
5. Inj. camphor in ether.	6 ampoules	15 ampoules
6. Inj. emetine ..	10 grains	25 grains
7. Inj. glucose saline, 5%.	20 pints	50 pints
8. Inj. quinine bi-hydrochlor.	12 ampoules	30 ampoules
9. Inj. morphine hydrochlor.	4½ grains	12 grains
10. Kaolin ..	2 lb.	5 lb.
11. Liq. paraffin ..	1 lb.	2 lb.
12. M&B 693 ..	150 tablets	375 tablets
13. Mag. sulph. ..	2 lb.	5 lb.
14. Pot. brom. ..	1 lb.	3 lb.
15. Pot. permanganas	½ lb.	1 lb.
16. Quinine tablets ..	300 tablets	750 tablets
17. Sod. bicarb. ..	1 lb.	3 lb.
18. Sulphaguanidine	200 tablets	500 tablets
19. Sulphanilamide	500 tablets	750 tablets
20. Tr. iodine (methyl).	1 lb.	3 lb.
21. Vitamin tablets	1,000 tablets	2,500 tablets
22. Ung. hydrarg. ammon.	1 lb.	3 lb.
23. Ung. sulphur ..	1 lb.	3 lb.
24. Yeast or equivalent, e.g. marmite.	1,000 tablets	2,500 tablets
25. Zinc sulph. for eye drops.	1 oz.	2 oz.

#### Surgical

1. Bandage ..	1 than	3 thans
2. Lint ..	1 lb.	3 lb.
3. Infusion apparatus	1	2
4. Wool ..	2 lb.	5 lb.

#### Disinfectants

1. Bleaching powder	50 lb.	125 lb.
2. Soap ..	8 cakes	20 cakes

#### 'Chronic' hospitals

Drugs	Amount for a fortnight for 50 beds
1. Acid boric—zinc-starch powder ..	2 lb.
2. Ammon. carb. ..	1 lb.
3. Aspirin (5-grain tablets) ..	350 tablets
4. Aqua dist. (double dist. for i.v. use)—ampoules of 5 c.c.	50 ampoules
5. Bismuth carb. ..	3 lb.
6. Calcium lactate ..	2 lb.
7. Carbon tetrachlor. ..	25 c.c.
8. Carbarsone tablets ..	150 tablets
9. Chloroform (pure) ..	1 lb.
10. Castor oil ..	10 oz.
11. Dettol ..	5 oz.

## APPENDIX I—concl'd.

## Drugs

Amount for a  
fortnight for  
50 beds

12. Ext. ergot liquid .. ..	1 oz.
13. Ext. kurchi .. ..	20 oz.
14. Ether .. ..	1 lb.
15. Ferri. sulph. .. ..	1 lb.
16. Glucose pulv. .. ..	3 lb.
17. Glycerine .. ..	2 oz.
18. Gum acacia .. ..	10 oz.
19. Hydrarg. subchlor. .. ..	1½ drams
20. Hypertonic saline tablets .. ..	75 tablets
21. Inj. atropine .. ..	1 tube
22. Inj. calcium gluconate .. ..	10 ampoules
23. Inj. camphor in ether .. ..	12 ampoules
24. Inj. emetine .. ..	50 grains
25. Inj. glucose saline, 5% solution .. ..	20 pints
26. Inj. morphine sulph. .. ..	5 grains
27. Inj. pituitrin .. ..	5 c.c.
28. Inj. quinine bihydrochlor. .. ..	100 ampoules
29. Kaolin .. ..	3 lb.
30. Liq. arsenicalis .. ..	1 oz.
31. Lysol .. ..	8 oz.
32. M&B 693 .. ..	600 tablets
33. Mag. carb. Levis .. ..	2 lb.
34. Mag. sulph. .. ..	5 lb.
35. Phenol .. ..	1 oz.
36. Pot. brom. .. ..	10 oz.
37. Pot. citras .. ..	2 lb.
38. Pot. iodide .. ..	2 lb.
39. Pot. permanganas .. ..	3 oz.
40. Protargol or argyrol .. ..	23 grains
41. Quinine sulph., pulv. .. ..	2 lb.
42. Quinine sulph., 5-grain tablets .. ..	1,400 tablets
43. Santonini .. ..	2 oz.
44. Sodi bicarb. .. ..	2 lb.
45. Sodi chlor. tablets .. ..	50 tablets
46. Sulphonamide tablets .. ..	600 tablets
47. Sulphaguanidine tablets .. ..	600 tablets
48. Spt. ammon. aromat. .. ..	2 oz.
49. Spt. methylated .. ..	1 pint
50. Spt. rectificatus .. ..	4 oz.
51. Urea stibamine .. ..	10 grammes
52. Tr. belladonna .. ..	2 oz.
53. Tr. card. co. .. ..	2 oz.
54. Tr. digitalis .. ..	2 oz.
55. Tr. iodine (methyl) .. ..	½ lb.
56. Tr. opii .. ..	2 oz.
57. Ung. chrysophanic .. ..	1 lb.
58. Ung. hydrarg. ammon. .. ..	2 lb.
59. Ung. sulphuris .. ..	2 lb.
60. Vin. ipecac. .. ..	1 lb.
61. Vitamin tablets .. ..	1,500 tablets Ex-
62. Yeast tablets (or solution) .. ..	1,500 tablets clude.
63. E.C. .. ..	4 bottles

## Apparatus

1. Cholera apparatus .. ..	1
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## Disinfectants

1. Bleaching powder .. ..	1 cwt.
2. Carbolic, 5% .. ..	10 cakes

## Medical News

## SUPPLIES AND DISTRIBUTION OF PENICILLIN

(STATEMENT BY MEDICAL RESEARCH COUNCIL)

It is now generally known in the profession, and even to some extent among the laity, that penicillin has remarkable therapeutic properties, and frequent inquiries are made about its availability. The following is a statement of the present position. In order to extend and amplify the pioneer work of Professor Fleming, and of Professor Florey and his colleagues at Oxford, the Medical Research Council, at the request of the Ministry of Supply, last March appointed

a Committee on Clinical Trials of Penicillin, which controls the distribution of penicillin for purposes of clinical research, and is instructed to employ the present limited supplies to gain new knowledge of the curative possibilities of the drug rather than merely to repeat the therapeutic successes of which it is already known to be capable. In addition to a quantity allocated to the War Office for trial in wounds in the Army overseas, supplies of penicillin for research into the systemic treatment of selected infections have been allocated to four centres in this country; four others are receiving, or are about to receive, smaller supplies for the study of local treatment only. It has not seemed advisable at present that these centres should be made generally known, nor that an invitation should be issued to refer suitable cases to them, because the numbers of patients which can be dealt with are so limited that this could only cause widespread disappointment.

The policy of the therapeutic trials now proceeding is to treat conditions known to be susceptible only so far as is necessary to define the minimum effective dosage, the best methods of administration, and any factors not yet studied on which success may depend, and to explore the possibilities of penicillin treatment in conditions hitherto unstudied from this point of view. Penicillin is known to have an action on many species of bacteria, some of which cause a great variety of lesions; these, together with the many forms which an infected wound may take, afford a wide field of study.

Even with the fullest co-operation of the Ministry of Supply and of the manufacturing firms, the difficulties in making penicillin on a commercial scale are still so formidable that the present output in this country is scarcely sufficient for the work in the four main research centres, and is only a minute fraction of the quantity which would be required if all cases of even a few specified infections were to be afforded treatment. Production on a greatly increased scale is being urgently undertaken both here and in the United States, but in both countries the requirements of the fighting services are likely to absorb most of the output for some time to come, and to name a date when adequate supplies will be available for general use is at present impossible. For the reasons given above it will be appreciated that requests for supplies of penicillin for the treatment of individual patients cannot, under existing conditions, be met.

Abstracted from the *British Medical Journal*, 28th August, 1943.

## BRITISH SURGEONS' VISIT TO U.S.S.R.

(IMPRESSIONS OF SOVIET MEDICAL ORGANIZATION)

THE four British surgeons, Surgeon Rear-Admiral G. Gordon-Taylor, consulting surgeon to the Royal Navy; Mr. E. Rock Carling, consultant adviser to the Ministry of Health, the Ministry of Home Security, and the Ministry of Pensions; Major-General D. C. Monro, consulting surgeon to the British Army (War Office); and Mr. R. W. Watson-Jones, civilian consultant in orthopaedic surgery to the Royal Air Force, paid a three weeks' visit to Soviet Russia and inspected hospital arrangements as far forward as Vyazma on the Western front, visited the clearing field, and mobile hospitals, and inspected the medical institutes and depots in Moscow. They found the organization of Russian medical services excellent. In their surgical work the Soviet medical service, with some differences in detail, follows the same general principles as those accepted in British war surgery, and has reached the same conclusions. The Commissar in charge of the service stated that at the time of the last war the Russians realized that their arrangements were not as good as those of their allies and during the twenty-five years between the two wars they have set themselves to reach a standard of medical and surgical work which will bear comparison with that of any other belligerent country.



## TWO IMPRESSIVE ORGANIZATIONS

Two points impressed the mission very greatly. One was the system of blood transfusion, which is carried out on a colossal scale. The arrangements for the collection of blood are beyond criticism, and the number of voluntary donors is very large. In one institution in Moscow a daily average of 500 to 800 donors are bled, and 90 per cent of them are women. No woman is allowed to be bled more than seven times a year. But in practice, so large is the number of volunteers, they are not bled more than five times. They receive extra rations and also payment, but four-fifths of the money received is returned for war purposes. The same procedure is followed as in this country in the use of plasma and serum. In no circumstances has the Russian Army lacked transfusion blood. The blood is transported to the front by large aeroplanes and then to outlying parts by small aeroplanes. At one place on the front blood has actually been flown to small collections of wounded behind the German lines. The second point was the organization for getting special cases into the hands of specialists at the earliest possible moment and in the condition in which they liked to receive them. Even as near to the front as eight or ten kilometres the different kinds of cases according to the nature and location of the injury are segregated and placed in the hands of junior specialists, who, after early treatment, pass them on to their seniors at the special hospitals. There appears to have been no shortage of dressings or anaesthetics. The Russians rely almost entirely on local and spinal anaesthesia.

## TRAINING OF PERSONNEL

As for the medical personnel, the chief of the medical services of the Russian Army, General Smirnov, is 35 years of age, and an expert opinion on him given by an academician was that he not only was an admirable administrator but was held in the highest regard by his colleagues from the professional point of view. The medical service is becoming a woman's service; 90 per cent of the doctors now under training are women, as compared with 50 per cent in peacetime. The mission noted that some of the young women doctors carried as many as five wound stripes, which meant, not that they have received five wounds, but that they had been wounded five times. For doctors in Russia the ordinary course before the first State qualification is five years, comparable with our own requirement. It takes three years to get a bachelorship and three more years to get a doctor's degree. Nurses had three years' training before the war, and this is now reduced to two years.

The Russian nurse evoked the great admiration of the visitors. Not only is she excellent at the job for which she has been trained, but she can turn her hands in spare time to any employment, even to building hospitals, involving cutting down trees, squaring timber, making window and door frames, digging out foundations. She is specially expert in the art of camouflage. One of the members of the mission described how their car stopped at a place in the forest where, apparently, no building was in sight. Slowly it dawned upon them that they stood at the entrance to a 1,000-bed hospital so camouflaged as to appear part of the forest itself. Some of the trees had even been left standing inside the building, their tops growing out of the roof.

The visitors saw something of the research institutes and medical organization in Moscow, where the civil defence and ambulance arrangements impressed them. Five telephone operators are detailed every night to deal with emergency medical or surgical calls from any part of the city, and within two minutes of the receipt of the call a well-equipped ambulance, with doctor, nurse, and orderly, is on its way. In the control room there is an immense map of Moscow; on receipt of a call a button is pressed for the name of the street, and the street then appears illuminated on the map, and the nearest ambulance station and the quickest route are at once indicated.

Abstracted from the *British Medical Journal*, 14th August, 1943.

## THE INDIAN HONOURS LIST

1ST JANUARY, 1944

THE following are the names of medical men, and others associated with medical institutions, in the Indian Honours List of date 1st January, 1944. We offer them our congratulations.

## C.I.E.

Colonel T. C. Boyd, I.M.S., Inspector-General of Civil Hospitals, United Provinces.

Lieutenant-Colonel A. S. Fry, I.M.S., Professor of Operative Surgery, King Edward Medical College, Lahore, Punjab.

Lieutenant-Colonel A. D. White, I.M.S. (Retired), Bengal.

## O.B.E. (Civil Division)

Lady Margaret Wilkie Bhoze, M.A.E., Central India.

H. Hawley, Esq., Government Analyst, King Institute of Preventive Medicine, Guindy, Madras.

## M.B.E. (Civil Division)

R. N. Bhandarkar, Esq., A.R.P. Divisional Warden, Dadar West Division, Bombay.

## Kaisar-i-Hind Gold Medal

Miss Dora Chadwick, Principal Matron, Surgeon-General's Office, Madras.

Miss Jean Murray Orkney, W.M.S., Director, Maternity and Child Welfare Bureau, Indian Red Cross Society, New Delhi.

Lieutenant-Colonel B. F. Eminson, I.M.S. (Retired), Civil Surgeon, Karachi, Sind.

Major R. A. Haythornthwaite, I.M.S., Civil Surgeon, Khasi and Jaintia Hills, Assam.

J. Lowe, Esq., Co-ordinator of Research, School of Tropical Medicine, Calcutta.

## Kaisar-i-Hind Silver Medal

Sister Mary Appollonie, Matron, General Hospital, Cuttack, Orissa.

The Reverend Mother Mary Augustine, of the Ursuline Order, Head Nursing Sister, Ranchi Sadar Hospital, Bihar.

M. L. Agarwal, Esq., Medical Officer, Mohan Eye Hospital, Aligarh, United Provinces.

## Kaisar-i-Hind Bronze Medal

Mrs. Elizabeth Ann Alley, Matron, Chittagong Railway Hospital, Bengal.

Miss Ethel Butchart, Matron, Ramsay Hospital, Naini Tal, United Provinces.

Mrs. Audrey Davidson, Voluntary Organizer, Blood Bank for the Jalpaiguri District and the Dooars, Bengal.

Mrs. Phyllis Mackenzie, Vice-President, Baluchistan W.V.S.

Miss Molly Mullane, Second Nursing Sister, European Hospital, Ranchi, Bihar.

S. Angami, Esq., Sub-Assistant Surgeon, Kohima, Naga Hills, Assam.

L. G. Nargund, Esq., Medical Practitioner, Kerur, Badami Taluka, Bijapur District, Bombay.

R. R. Ayvar, Esq., Health Inspector, Madras.

## Bar to the Kaisar-i-Hind Bronze Medal

G. S. Rao, Esq., Health Inspector in-charge of Malaria Field Station, Krishnadevipeta, Vizagapatam District, Madras.

## Khan Bahadur

M. Yusuf, Esq., Professor of Clinical Medicine, King Edward Medical College, Lahore, Punjab.

Khan Sahib S. A. Khan, Superintendent, Provincial Tuberculosis Sanatorium, Dadar, North-West Province.

## Rai Bahadur

R. Dutt, Esq., Civil Surgeon, Howrah, Bengal.

B. M. Das Gupta, Esq., Professor of Protozoology and Director, School of Tropical Medicine, Calcutta, Bengal.

J. C. Chatterjee, Esq., Superintendent, Calcutta Medical School and Hospital, Bengal.  
 Rai Sahib M. Ganguli, Medical Practitioner, and Honorary Physician, Out-patients' Department, Mayo Hospital, Calcutta, Bengal.

S. N. Ganguli, Esq., Civil Surgeon, Palamau, Bihar.  
 S. N. Acharya, Esq., Civil Surgeon, Balasore, Orissa.

#### Rao Bahadur

G. D. R. Gnanamuttu, Esq., Civil Assistant Surgeon and A.R.P. Casualty Officer, Madras.

A. S. Nayudu, Esq., Professor of Medical Jurisprudence, Medical College, and Police Surgeon, Madras.

Rao Sahib T. M. Vakil, Medical Officer, West Hospital, Rajkot.

#### Khan Sahib

Maulvi Z. Ahmed, Demonstrator of Anatomy, Dacca Medical School, Bengal.

#### Rai Sahib

S. C. Bose, Esq., Medical Officer, Palta Water Works, and Vice-President, Barrackpore Cantonment Board, Bengal.

G. C. Roy, Esq., Medical Practitioner, Chitpore Dispensary, Mayo Hospital, Calcutta, Bengal.

L. P. R. Puri, Esq., Civil Surgeon (Officiating), Lyallpur, Punjab.

S. P. Mukharji, Esq., Assistant Surgeon and Staff Medical Officer, A.R.P., Jamshedpur, Singhbhum, Bihar.

S. Misra, Esq., District Health Officer, Berhampur, Ganjam District, Orissa.

P. N. Dhandu, Esq., Medical Officer of Health, Quetta Municipality, Baluchistan.

M. L. Kapur, Esq., Sub-Assistant Surgeon, on Special Duty, Office of the Director-General, Indian Medical Service, New Delhi.

#### Rao Sahib

M. Sundaranathan, Esq., Lecturer in Pharmacology, Madras Veterinary College, Madras.

K. V. N. Nayar, Esq., Assistant District Medical Officer, Ootacamund, The Nilgiris, Madras.

M. B. Mandhale, Esq., Resident Medical Officer, J. J. Hospital, Bombay.

#### O.B.I.

To the First Class with the Title of 'Sardar Bahadur'  
 Indian Army Medical Corps

Subedar-Major Ganga Singhi, Bahadur, O.B.I.

Subedar-Major Ata Muhammad Khan, Bahadur, O.B.I.

Subedar-Major Shiv Ram, Bahadur, O.B.I.

Subedar-Major and Honorary Lieutenant Ladha Ram, Bahadur, O.B.I.

Subedar-Major Maniklal Motilal Talati, Bahadur, O.B.I.

Subedar-Major Narindar Singh, Bahadur, O.B.I.

Subedar-Major and Honorary Captain Rai Sahib Madho Parshad, Bahadur, O.B.I.

Subedar-Major and Honorary Captain Kartar Singh, Bahadur, O.B.I.

Subedar-Major Hari Krishan Gupta, Bahadur, O.B.I.

To the Second Class with the Title of 'Bahadur'  
 Indian Army Medical Corps

Subedar-Major Mathura Das.

Subedar Ram Saran Mehra.

Subedar Sunder Singh.

Subedar Yaqub Ali.

Subedar-Major Muhammad Ismail.

Subedar Prem Roy Farsuram Pandya.

Subedar-Major Balwant Singh Bindra.

Subedar-Major Kishan Singh Sumra.

Subedar Indar Singh.

Subedar-Major Hardayal Singh.

Subedar Muhammad Shafiq.

Subedar Dayal Singh.

Subedar-Major Dhari Ram Bhatia.

Subedar Sardar Sahib Sapuran Singh.

Subedar-Major Uddham Singh.

Subedar-Major Atma Ram.

Subedar Rajindar Singh.

Subedar Mohan Lal.

Subedar Gurbachan Singh Sethi.

## Current Topics

### Air Raid Casualties

By N. E. JAMES, M.B., B.S. (Lond.)  
 (From the *Journal of the Christian Medical Association of India, Burma and Ceylon*, Vol. XVIII, November 1943, p. 303)

IN talking of one's experiences as a Medical Officer in the London 'Blitz', it may help if I just briefly tell what happened in an ordinary city hospital up to the time the 'Blitz' began. Away back in 1938, there was the crisis about Czechoslovakia. The hospitals had hurriedly arranged plans with their inadequate military and medical equipment for the trials of aerial bombardment. The authorities of the hospitals were very relieved when Mr. Chamberlain brought back from Munich the paper, on which was Hitler's illegible signature, declaring the peaceful intentions of the *Fuehrer*, but at the heavy price of Czechoslovakia. One remembers the tense groups listening in to the radio, the distribution of gas masks to the privileged few, the panicky news from the business world during those days.

#### 'BRITAIN REARM'

During the rather fitful breathing space of the next year, Britain did her best to rearm herself for the conflict which seemed to be coming. The Air Force increased their fighter planes from the squadron or so they possessed at the time of 'Munich' to the hundreds that were ready to repel the invading Luftwaffe in the Battle of Britain in 1940. The hospitals of London, as well as those of Great Britain, had many important conferences and committees, planning, co-ordinating, arranging supplies, preparing should another international crisis threaten. A plan was devised for each of the teaching hospitals of London to control a sector of the medical facilities of the metropolis and the adjacent country side. In the summer of 1939, war clouds threatened, and the various preparations of the military and hospital authorities soon became evident. Searchlight practices; balloon barrage; convoys of army lorries, tanks and Bren gun carriers; air raid precautions; first aid classes; stretcher parties, rescue and demolition squads; gas decontamination facilities; all these were organized. Instructions about, and demonstrations of, dealing with incendiary bombs, air raid shelters in the home, and the gas proof room at home were made.

#### CRISIS 1939

As political relations deteriorated, black-out trials, distribution of gas masks and voluntary evacuation were arranged. In hospitals, patients were classified as to whether they could or need be evacuated. Each patient had his bundle of clothes, etc., gas mask, and case notes ready and tied to his bed, awaiting the evacuation order, medical students and others set to and dug up lawns and gardens, filling sandbags for protecting buildings. Steel supports were erected in important buildings to assist in the support of the main beams of the building, and all glass windows were protected by cellophane or netting strips. The operating theatres were transferred from the upper stories to the ground floor, and in our hospital, 'Matron's Office' had to be evacuated to accommodate them. Special alterations were made to render them gas proof and bomb proof.

#### EMERGENCY

About three days prior to the outbreak of war, the Government declared 'a state of emergency'. School children and hospital patients were evacuated to the country. The hospital published a list, whereby the nursing staff and medical staff were distributed among several suburban and country hospitals in its particular sector. Medical members of the Territorial army

disappeared from hospital practice or else lived constantly in uniform, reporting to their headquarters regularly.

3RD SEPTEMBER, 1939

The population was keyed up for a surprise military attack when Mr. Chamberlain announced over the Sunday morning radio on 3rd September, the declaration of war. Within half an hour of this announcement, the air raid sirens sounded the first warning of the war. Its effect was electric. People in the streets ran for shelters, mostly basements, with mob hysteria in our district. Panic stricken people clamoured for protection from the hospital, but a firm and wise rule published previously in the hospital said that only the injured and ill should be admitted in these circumstances. This alarm—a false one as it proved to be—lasted only a few minutes, but it gave the people some confirmation that a severe trial for them had already begun.

During the day, parties of the hospital staff left for various hospitals to which they had been appointed, some of them several miles out in the country. Expecting some tens of thousands of casualties that night, many of these people were alarmed to find how inadequately some of these hospitals were supplied. One of these hospitals had 200 beds and blankets, 2 artery forceps and 24 female silver catheters. It was fortunate that hostilities were delayed because in that time the proper organization and equipment of these hospitals were quickly attained. Within about two months most of these hospitals were able to admit and treat most medical and surgical cases adequately.

#### THE 'PHONEY' WAR, 1939-40

For some nine months the emergency services of A.R.P. in medical work and air raid protection were almost idle. The hospitals did little clinical work. Evacuees of all sorts drifted back to London. The folk who had been obliged to be hosts began to complain of their billetees. Various difficulties of personnel and personalities began to crop up. A very severe winter occurred and gave much trouble to travellers, disorganized sanitary arrangements, and produced many pulmonary diseases amongst service men. Clinical material became more plentiful and the emergency hospitals were used more and more for these service cases. In May, Germany advanced through Holland and Belgium, and the retreat from Dunkirk and the fall of France followed. The casualties from this operation were mainly distributed among the hospitals of the South Coast, and we saw only occasional cases from that evacuation.

In September, the Battle for Britain began in earnest. The wailing sirens used to go fairly regularly soon after dusk and the warning often would last till nearly dawn. The drone of planes coming and going continuing through the night; the rattling of windows, the quiver of buildings, with the explosion of distant bombs; the frightening 'snarl' of a diving bomber; the uncanny, penetrating, almost metallic 'swish' of the falling of a nearby bomb; the spluttering giddy whine of a stricken plane spinning to earth; the sinister low-pitched rhythmic purr of the German engines; the higher-pitched steady compelling note of the British Hurricanes; the muffled crack of anti-aircraft fire and then the rain of some of the shrapnel on the roof; the ominous dull thud and rumble of buildings collapsing; the clang of breaking glass; the commanding buzz of the telephone bell; the exasperated voices of the telephone operators trying to deal with delays and breaks on the line; the grinding of the brakes of ambulances as they drew up to the casualty door; the conversation and voices of a busy receiving room, the insistent demands of ambulance men for their blankets, the orders to porters, the busy voices of the nurses and the medical officers, the quiet, encouraging but firm voices of surgical chief or superintendent on their rounds; the staccato clatter of footsteps going up and down the wooden stairs; echoing footsteps and the creak of a stiff wheel of a theatre trolley trundling down a dim corridor; the bubbling

sterilizer, the splashing noise of water and lotion, the clink of instruments, the slap of plaster, the rhythmic buzz of anæsthetic valves, the intent voices of surgeons and assistants in the theatre; the clatter of china and silver, the din of gossip in the canteen; the jingling of bottles of blood against each other on the stand in the ward; the moan of a patient; the nurses reply; the jovial repartee of the convalescent; the 'cheerio' of the evacuee; the gasping of the moribund; the silence of the departed; this was some of the orchestra to whose accompaniment we worked and lived in those tragic days of history for London.

We listened to the pitiful stories of families pulverized, of people buried for days beneath debris, of folk trapped in underground shelters by fallen masonry and drowned by water from the fireman's hose trickling down into their shelter, and of small children orphaned. Fathers never knew when might be their turn to return to find their homes a heap of smoking rubble. There was that injured mother who still clung to the last remains of the son who had slept on her lap, now only a shattered skull; there were those 20 auxiliary firemen, who, exhausted from four days' and nights' continuous duty, slept on some railway station seats and never woke up again. From time to time, a hospital might be without any electricity or water or sewage system. Occasionally an army lieutenant used to come to borrow a stethoscope to diagnose the prognosis of a delayed action bomb, one of them under St. Paul's. At times we sent, at times we asked for, urgent supplies of blood, serum, spirit, instruments, surgeons, dressings.

Through all those trials we came to know the courage, the fortitude of the common British people, to know how much their culture was founded on spiritual principles, to know why it was they said—'We can take it'.

#### ORGANIZATION FOR AIR RAID CASUALTIES

Organizing a hospital for air raid casualties was somewhat different from that for peace time emergencies. Our constant aim was to provide the best possible treatment for each casualty, even in spite of difficult and changing circumstances. In busy times and in the stress of heavy work, our standards were often lowered but these difficulties were not accepted as any excuse for lowered standards. Plans were made elastic and at times were quickly changed. Mistakes had to be freely admitted and experiences constantly shared. The value of a regular (daily if necessary) conference of the leaders of departments about pertinent matters was commended to all busy hospitals. Hospitals had their several plans of organization, and the following is a typical one.

The valuable help which medical students gave to our hospital may not be possible everywhere, but some points on this plan may help others in their own hospitals. Some other hospitals, denied the help of medical students, gained the help of the Boy Scouts, St. John's Ambulance Association, the Red Cross, and similar bodies to help in stretcher-bearing, as tally-clerks for ambulances, stretchers and blankets, or as messengers between departments. To lighten the work of the bearers, as many wheel trolleys as possible were provided. Provision was made for: (a) reception of cases from the ambulance, (b) preliminary inspection of injuries in the receiving room and sorting of cases, (c) resuscitation, (d) operation, (e) subsequent treatment, (f) evacuation to base hospitals in the country, and (g) mortuary.

Personnel required in this hospital (equipped to cope with some 100 casualties) on night duty were: (a) acting medical superintendent, (b) surgical chief, (c) operating assistant surgeons for 3 to 5 tables, (d) staff physician on duty in the resuscitation ward and for consultation with the surgeon, (e) as receiving room officer—one of the specialist staff or an experienced resident, (f) anæsthetist—one specialist and a junior, (g) x-ray personnel, (h) house officers, (i) matron and nursing staff and secretaries, and (j) engineer, domestic staff, porters, stretcher-bearers, and fire watchers.

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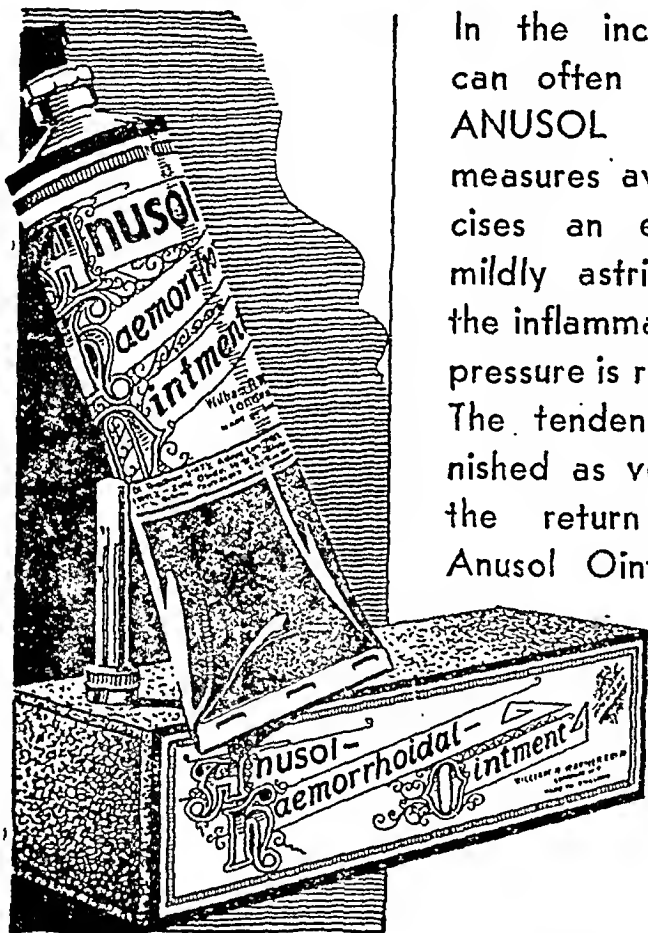
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1. *The acting medical superintendent* had special duties. A secretary sat in his office to receive any message, while a messenger was ready to contact him at any time, being informed of his whereabouts or going round with him. He must watch the rate of admission of casualties so that the capacity of the hospital for efficient surgery is not exceeded. He can telephone A.R.P. control, or contact the ambulances by means of the police, or tell the neighbouring hospitals that convoys must be diverted from his hospital. If communications are cut, a messenger can be sent by ambulance. He must make frequent rounds of the wards to encourage the staff and patients, he must visit other parts of the hospital to investigate any difficulty or incident from falling missiles. He may have to order the evacuation of a ward because of damage or of broken windows. He may have to call for help to deal with incendiary bombs or call the fire brigade. He must visit the theatre and the resuscitation ward to see that the staff are being relieved before they get unduly fatigued after an all night session. He must consult the surgical chief on policy, on pressure of work, on the number of casualties that can be evacuated next day, and on the rota of 'days-off' for the medical staff (an essential provision, we found).

2. *The surgical chief* had his own duties. He visited the resuscitation ward as soon as it began to fill. He must see that this ward has staff limited to an appropriate number to deal with the cases. As the shock is being treated he makes a systematic examination of each case, recording details of all injuries, and collaborating with the physician in charge in ordering transfusion and other therapy, and according order of operation and surgeon to each case. A portable x-ray was available for special needs. He must pay regular visits to the receiving room, and to the less serious cases in the wards, and arrange their operations to fit in with those recovering from shock. Serious cases must return to the resuscitation ward until recovery is assured. At intervals he must give advice in the theatre; he may operate there in slack times, on special cases, but this is *not* his first duty. Next morning he must assist the surgeons and the house surgeons to select cases for evacuation.

3. *The physician*.—His duties lay in the resuscitation ward, and he was responsible for all serious cases of shock, and for the important decision about length and time of transfusion. He must decide and arrange when fluids (oral, rectal, intravenous) and oxygen may be given to patients, when they can be removed to the theatre or another ward (a serious decision for shocked patients). He makes records of the readings of shocked patients—B.P., pulse rate, Hb per cent, fluids lost in vomiting and any blood lost. In a slack time, detailed observations on shock could be made for general clinical information. Both sexes were treated in the same ward as it saved staff and unified treatment.

4. *The receiving room officer*.—With the help of an adequate nursing staff, he must deal with admission of casualties. He must make a superficial examination to decide whether the patient is to go to the resuscitation ward, a general ward, or needs out-patient treatment. We tried to maintain a rate of dealing with some three or four cases in ten minutes. Some 50 to 60 per cent of cases require operation, about 25 per cent need treatment for shock in the resuscitation ward, which is best nearby the receiving room. Most cases needing x-ray examination could wait till day time, we found.

5. *Mortuary*.—Ten to twenty per cent of the casualties were dead either on admission or soon afterwards. Arrangements were made for a suitably sized mortuary, for any relatives to identify the bodies, and for their early removal to a public mortuary next morning. The tragic sackful of 'bits' that were collected overnight were also suitably destroyed.

*Evacuation*.—After a high number of casualty admissions during the night, evacuation of as many as possible was made next day. The best time for evacuation was at 2 p.m., when the night surgical staff had

gone to bed. For serious cases, a mattress and pillow were essential for the journey.

*Relief*.—A rota of relief surgical teams was arranged. The rota was drawn from the visiting staff of the hospital or from a hospital in the suburbs. The night teams stopped working at 8 a.m., and the reliefs continued at 10 a.m. With admissions controlled according to the capacity of the hospital, operations usually finished by midday. It was important that hospitals should not work themselves to a standstill before calling the relief teams, otherwise the relief teams found it difficult to work and co-operate with a staff 'laid out'. The most economical method proved to be that after a certain numbers of hours operating, the relief teams were automatically called.

Lectures and practices were given to the stretcher parties, gas and fire watching units. When there was no raid during the long winter evenings, social evenings were held, and were valuable in maintaining morale. The superintendent and the engineer must see that an adequate number of efficient fire buckets, sand bags for incendiaries, hoses and fire extinguishers were available at suitable points. At night we ran a canteen where refreshment for hospital staff, fire watchers, stretcher and ambulance men, police and firemen was available. The theatre staff should have half an hour off between midnight and 3 a.m. if operating had begun early. We found that all windows of important offices and services, operating theatres, the receiving room, the resuscitation ward, and connecting passages, should be bricked up. They are best all situated on the ground floor.

Reserve water supplies, heating, lighting were always kept in readiness. All the alternative exits from the wards and from the hospital were kept in good order and well known to all, especially sisters, house officers and stretcher parties.

This was the plan for a large hospital; smaller hospitals adopted different plans, mostly following the same principles, and especially, that shocked patients should be treated at once by special staff in a special ward near the receiving room, and that the senior surgical opinion should examine and classify all casualties, most operations being done by assistant surgeons.

#### FIRST AID

At the beginning of the war, great emphasis was placed on efficient first aid to the casualties, but we soon found ourselves agreeing with Trueta of Barcelona that first aid treatment should be of the simplest and that the best first aid is done in a hospital operating theatre. The only time a tourniquet need be applied is in a case of traumatic amputation of a limb. Most other bleeding wounds respond well to a firm dressing. Tourniquets were usually put on badly, often enough by relatives and bystanders. In the darkness they were difficult to put on properly and the constriction caused arterial and increased venous bleeding, and more shock. Also a wound whose blood supply has been cut off by tourniquet or injury presents a nice medium for the growth of all sorts of pyogenic bacteria, and especially for *Clostridium welchii*, which is responsible for gas gangrene. The only injury that needs to be splinted is a fractured patella. Fractures of the leg can be controlled by tying both legs to a rolled blanket, while fractures of the arm can be quickly and temporarily treated by tying the injured arm to the trunk.

The general practitioner in charge of rescue squads and first aid parties, was usually the first to see the casualties, and he was also responsible for the order with which casualties were taken to hospital by ambulance. Patients with shock, abdominal and chest wounds were sent first generally, while head wounds and compound fractures followed soon after. Lesser injuries were sent later.

The casualties were admitted to hospital grey with dust, from being buried under brick and masonry debris, often for many hours, and often grey with shock. Many of the cases other than abdominal injuries revived a good deal after drinking a big cup



of hot sweet tea. We found this a valuable first aid measure.

Before dealing with the classification, let me say a few words about the types of injury inflicted on the victims, and the relative mortality.

The air raids occurred sometimes in day time, more commonly at night. During the day time, the air raids were usually short and sharp, high explosive and incendiary bombs being dropped on streets, houses and factories. People were caught in the streets or shops or factories, all relatively unprotected compared with the shelters, in basements of concrete buildings or the strong surface shelters where they often were at night. Each bomb dropped in day time caused a larger number of casualties than one dropped at night. Also the mortality of the day-time casualties was higher than at night. The mortality of the day casualties was about 20 per cent, while at night the mortality was about half this. This may be partly explained by the fact that the day-time incident usually produced blast and bomb splinter wounds and the casualties were quickly taken to hospital. Here many of the seriously injured died. At night, when a building was hit (the common night incident), the injured dead lay buried under the debris of the collapsed building. It takes time for the rescuers to reach all the casualties and some of the seriously injured died under the debris. Other casualties up to about 75 per cent of the total had glass injuries, of which a large proportion were not serious, while the remainder had crushing and other injuries from falling beams and debris.

The most severe injuries were those penetrating wounds due to primary missiles, i.e. high velocity bomb fragments, and the larger crush injuries due to falling masonry. Secondary missiles of low velocity, e.g. glass and wood and bricks, produce less serious wounds.

The severity of the bomb splinter wound is due to the velocity of the splinter—something like 3,000 to 5,000 feet per second. In civil practice, penetrating wounds are due to objects of small momentum, with only a small area of damage around the track, whereas with the high velocity splinter, a large area of tissue of precarious vitality is produced around the missile track, due to the momentum imparted to the tissues by the high velocity missile. On the presence of this contused devitalized muscle mass depends much of the new principles in war surgery.

#### BLAST INJURY

Special investigation of these injuries has been made in this war.

Zuckerman has shown that, except for large bombs, blast is not experienced further than 20 feet from an explosion. The wave of pressure drops rapidly and becomes normal 30 feet from the explosion. The blast consists of a rapid and intense compression wave followed by a rather slower suction wave. The damage to the human organism may consist of lesions in lung, C.N.S. or abdomen and the lesions are hæmorrhagic. The lungs may show hæmorrhages at the periphery of the lung, as intercostal markings in children, as lesions at the phrenicocostal sinus in adults, often with damage to liver or spleen also, and occasionally with a hæmatoma at the root of the lung. Dyspnoea and venous congestion are the main symptoms, and are treated best by an oxygen mask (B.L.B. or Rose and Sellors mask) or tent, and venesection. The hæmorrhage may continue for 4 hours after injury, so that artificial respiration as first aid should never be done to those cases, as, by so doing, further hæmorrhage may occur.

In the abdomen, pain and blood in the motions for a few days or occasionally serious hæmorrhage and laceration may occur from blast injury. In the brain, hæmorrhagic and contusion lesions may occur, the commonest being a subarachnoid, cerebral or spinal hæmorrhage, causing various degrees of coma and a sometimes transient paralysis. Blast effects have occurred at sea, and men immersed in the sea near an explosion, have suffered from these lesions. The action of the blast seems to be purely a concussion on the external surface of the body, as the side of the

body which is nearest the explosion suffers most. This injury is not common and it was often confused with a state of dyspnoea caused by powdered dust, bricks and other debris in the nasopharynx and trachea.

#### FALLING MASONRY

Injuries from this cause were plentiful—either crushing or penetrating in type. The most common penetrating missile was glass, found in about 75 per cent of casualties. Many of the serious crush injuries never reach hospital alive.

#### BURNS

Burns were of various nature and occurred in all parts of the body. Burns of hands and face were closely studied because of the unhappy results accruing from simple tannic acid treatment.

A classification of casualties in common use was as follows:

1. Cases needing operation.
  - A. *At once.*
    - (i) Primary hæmorrhage.
    - (ii) Abdominal injury.
      - (1) Penetrating wound, by anterior or posterior route, or through the buttock.
      - (2) Contusion or crush injury.
      - (3) Some cases of blast injury.
    - (iii) Open pneumothorax.
  - B. *At an early convenient time.*
    - (i) Most lacerations, penetrating wounds, and compound fractures without shock.
    - (ii) Suitable open head injuries.
  - C. *After resuscitation—on recovery.*
    - (i) Lacerations, wounds and compound fractures with shock.
    - (ii) Burns.
2. Cases not needing operation.
  - A. *Without much external injury.*
    - (i) Through and through wounds of the chest.
    - (ii) Simple shock and blast injuries.
    - (iii) Abrasions and contusions. Simple fractures.
    - (iv) Foreign body in the brain (scalp needs suture).
  - B. *With much external injury (hopeless cases).*
    - (i) Large wounds of abdomen with prolapsed viscera.
    - (ii) Large skull wounds, and brain damage.

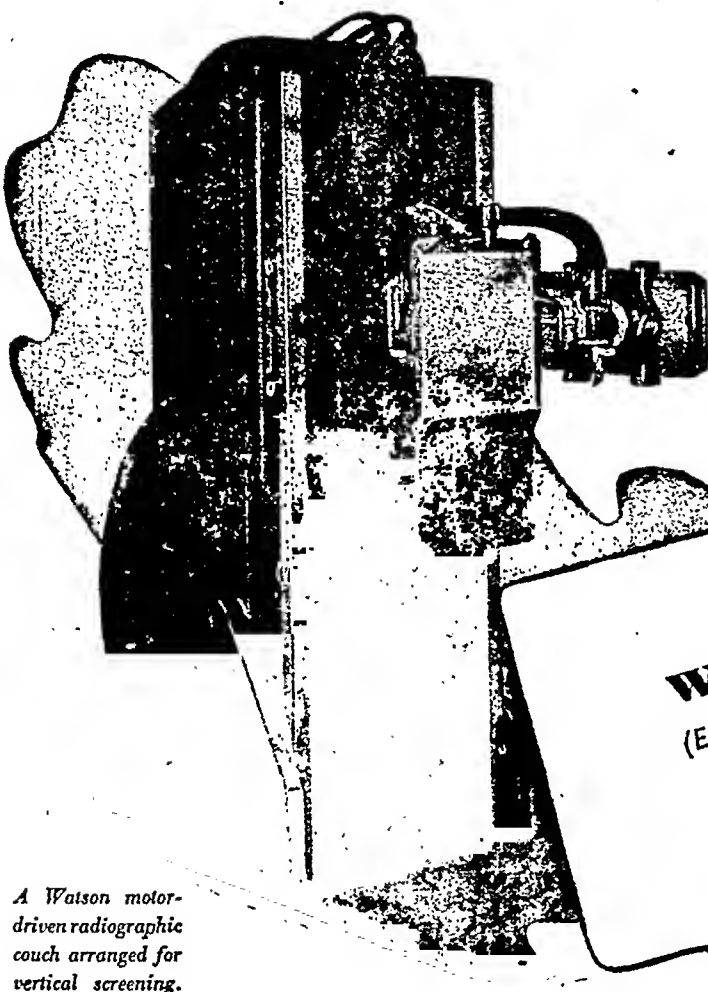
#### TRAUMATIC SHOCK

This was a problem to which much information was contributed by the clinical study of air raid casualties. Shock, a product of a variety of conditions, is a clinical syndrome which often appears after trauma. The patient's B.P. is usually low, the pulse is often rapid, and there is pallor and sweating.

The ætiological factors may be classified as follows:

1. *Fright*—emotional shock—may cause collapse in a person. The help a cup of tea gave to this type of patient was well known. They quickly recovered.
2. *Post-traumatic hypertension*.—Although suffering from a recent injury, some patients may show a raised blood pressure, even though they are not cases of chronic hypertension. The pulse is thin and thready, there is pallor and sweating. In this group expectant treatment is adopted for they may recover completely or develop into other types of shock (see below).
3. *Neurogenic shock*.—A patient may collapse from excessive nervous stimulus from severe pain or cold. (During a Commando raid on Norway, a British Bomber was brought down by A.A. fire into the icy sea. Although a rescue ship was at the spot within 20 minutes, all the men were dead soon after rescue, from shock from cold). In this type of shock the pulse is usually slow, but the B.P. is low. The syndrome resembles a vaso-vagal attack, and is compatible with a blood loss of some 1 to 1.5 litres. When this type of shock is associated with brain injury, the outlook is very serious.

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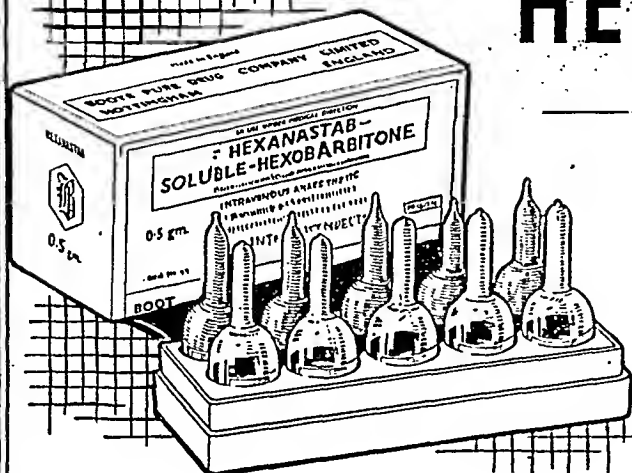
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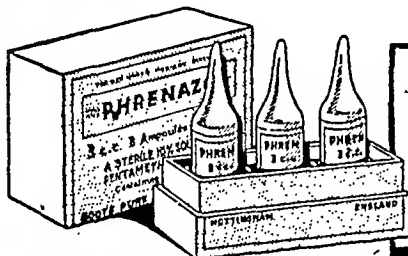
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4. *Oligæmic shock*.—This is due to loss of circulating fluid from:

- (a) Blood loss—the pulse may be *normal or rapid*; the hæmoglobin, although 80 to 90 per cent soon after the injury, will fall to a low level in a few days.
- (b) Plasma loss—as in burns and crush injuries.
- (c) Both (a and b) combined. In this case the patient is unable to retain transfused plasma or serum in the circulation.

This is the most important type of shock. We experienced several tragedies before it was realized that the pulse rate is quite deceptive. The B.P. is much better, and is essential for control of treatment. The B.P. may confuse however, as in type 2 above, and in fact that in some cases of fright, there is a transient low B.P. A clinical appraisal of the severity of the injury, the amount of blood lost, together with the B.P. reading is the best guide to the degree of oligæmic shock. Simple measures are useful in all cases, such as blocks under the foot of the bed. Severe shock reacts best to a blood transfusion, or, nearly as good, a plasma or serum transfusion. Saline has no real place in the intravenous therapy for shock, indeed it may tip the balance against the patient, by washing out the plasma proteins from the circulation into the damaged tissues. Two pints of blood or plasma must be given rapidly, the first pint in 15 minutes, the next more slowly, and then continue transfusion (best with blood) until the B.P. rises to 100 mm. Hg. or more. For the first pint, some pressure may be needed to assist the transfusion. Later transfusion is best given slowly as transient rises of B.P. are thereby avoided. *The lower the initial B.P., the more urgent is the transfusion.* Treatment must be begun early, as every delay in commencing means a more prolonged and uncertain resuscitation. If there is no B.P. response from 2 to 3 pints of blood, and no bleeding is evident or suspected, the outlook is hopeless. Also if the B.P. is under 80 systolic for 2 to 3 hours, the prognosis is also hopeless.

The optimum time for operation is the earliest moment after the restoration of the B.P. to 100 mm. Hg. At operation the aim was to do a little quickly, and continue the transfusion. The critical level of the B.P. is 80 to 90 mm. Hg., of Hb. is 50 per cent; when blood transfusion is necessary to save life. Morphina we found is required only when pain returns and is rarely necessary, indeed it may be harmful if given at the outset. A warm skin holds some  $\frac{1}{2}$  litre more blood than cold. To a patient in a critical condition application of warmth may be very damaging to his general metabolism, diverting valuable blood from vital centres to the skin. Therefore warmth was applied only when the B.P. was improving in the recovering patient.

5. *The crush syndrome*.—When a person had been imprisoned in debris for some hours, with one of his limbs pinned under a heavy beam, he was very liable to succumb to a syndrome of shock and renal failure called 'the crush syndrome'. We saw a few cases of this syndrome. Characteristically there is severe shock, relieved with difficulty by some 2 days' transfusion; only to be followed a day or so later with 3 to 4 days' anuria, with a steep rise of blood urea, and sometimes death. Severe oedema, sometimes gangrene, developed in the injured limb, but amputation seemed to be of no help in preventing the syndrome. More recently a plaster or an elastic bandage applied to the limb as soon as possible after its release from the crushing beam seems to have produced better results. This syndrome seems to be caused by toxic products from the crushed, devitalized tissues of the injured limbs, especially when the blood supply of the damaged limb is constricted or cut off by the crushing effect of the heavy beam.

6. *Circulatory collapse may produce a 'shock syndrome' as in*

- (i) Fat embolism from fat globules set free into the circulation at the site of injury, producing lesions in brain or lung.

- (ii) Pulmonary embolus.
- (iii) Coronary thrombosis.

#### MEDICAL DISEASES

Besides casualties, wartime illnesses were treated. Duodenal ulcers were common, and cases of perforated ulcer were not uncommonly encountered in the middle of an operating list. Most cases of neurosis evacuated themselves to the country voluntarily, and only a few serious cases were seen. The fellowship of the folk in the shelters and underground station shelters helped considerably in preventing more widespread mental upsets. Skin diseases and various infestations were prevalent until proper supervision of shelters was made. Pleural effusions of simple nature were a common illness amongst shelterers. Tuberculosis increased in incidence due to the crowded shelter life at night. Oedema of legs and femoral thrombosis, sometimes pulmonary embolisms, occurred from the pressure of bars of deck chairs, which were so commonly used by people in the shelters.

#### ANÆSTHESIA

Inhalation anæsthesia was commonly used, gas oxygen and ether being most popular. Some good results were recorded after use of the modern anæsthetics such as Cyclopropane and Dichlorethylene. These were used more especially with novocaine regional anæsthesia in the abdomen and elsewhere. Spinal anæsthesia was hardly ever used, because of the risk of shock recommencing. Barbiturates, especially Pentothal, were used from time to time, but with variable results; some reported that it produced more shock, but this may have been due to other factors. Recently both in England and the Middle East, Pentothal has been used with good results for casualties resuscitated from shock.

#### OPERATIVE PRINCIPLES

Theatres had 3 to 4 tables usually, and one instrument assistant looked after two of them. The principles of war surgery are largely those of traumatic surgery. Let us remind ourselves of a few. In treatment we are faced with one or more or a combination of three tasks:

- (i) The saving of life from shock, hæmorrhage or injury to vital organs.
- (ii) The prevention of sepsis (and ultimately to save life)—the commonest problem—in lacerations, etc.
- (iii) The prevention or correction of deformities, as in fractures, burns, and nerve and tendon injuries.

The treatment may be conservative—as in treating shock or sepsis by drugs, sera or transfusion; or operative—as in control of hæmorrhage, excision of wounds or manipulation of fractures. Most of the air raid surgery came under group (ii).

#### THE TREATMENT OF LACERATED WOUNDS

Let us consider the commoner lacerations. These lacerations were very dirty. Street dirt, grime and blood were often ground into their clothing and skin, and even more so into the depths of the wounds, and provided an excellent source of sepsis. If, in addition, the viability of the muscle adjacent to the track had been endangered by a high velocity missile, special care in the operative treatment was necessary. Trueta, in his large experience of casualties in Spain, led the way in the modern treatment of these wounds. Based on his principles, our common practice in wounds was:

1. Surgery must be prompt, and within six hours, if possible. If adequate surgery can be done within twelve hours of injury, much time may be saved for the patient and for the hospital. If within six hours, the majority of wounds treated by adequate surgery will quickly heal without incident. After 12 hours usually the wounds are potentially infected. *The severity of the post-traumatic infection is proportional to the post-traumatic interval.* First-aid parties must learn the new duty of getting the patient to hospital in the shortest time possible. Time-consuming procedures of

splinting and bandaging must be forgotten for air-raid casualties. Inhalation anaesthesia, using gas and oxygen, ether or chloroform is best and only a little is usually necessary. For severe shock, local anaesthesia may be used.

2. Clean the wound with soap and water; eoeonut and castor-oil soaps are more effective in ridding wounds of the collection of bacteria and microscopic dirt and debris than the strongest antiseptics. Dettol and similar antiseptics are the only alternative. The soap and debris are washed away by a stream of saline, the skin being shaved for a good distance around the wound.

3. Without proper excision, no recent wound should be enclosed in plaster, otherwise failures occur. Wounds not yet 12 hours old should be completely excised, together with adequate removal of all devitalized tissues and foreign bodies, exploring and enlarging all tracks. Wounds over 12 hours old potentially infected, should have the surgery limited to free drainage and removal of obviously dead tissues. Wounds up to 6 hours old can be sutured successfully after a proper excision, but there must be no deep sutures, otherwise sepsis is liable to occur. In military surgery of the Middle East, it has been found better to pack all wounds, and this is a safe rule in the surgery of casualties too.

4. *Excision.*—Enlarge the wound first, excising a *thin* piece of skin. Wounds from high explosives cause more damage deeper than at skin level. Specially attend to the excising and enlarging the hole in the *deep fascia*, incising skin and deep fascia longitudinally up and down the limb, and transversely too, if the muscle wound demands it. (A high explosive missile produces wounds in skin and fat, and in muscle, larger than its own size; but the wound in the deep fascia is usually about the same size as the diameter of the missile.) After dealing with the deep fascia, 'saucerize' the wound by excising dead tissues, especially muscles, till the bottom of the wound is reached, proceeding layer by layer. Don't incise the periosteum, only remove any loose bone. Pack sulphanilamide powder into the wound, emulsifying it with the tissue fluids there.

Drain the wound by packing gauze (plain, vaseline or flavine) into the depths of the wound, firmly but not too tightly. Some wounds, especially those with a deep narrow cavity at the bottom of the wound, need counter drainage by providing an opening for drainage in the most dependent part of the wound. The limb is then immobilized in plaster, a good absorbent of the discharges. Immobilization in plaster does best if the wound has been completely excised within 6 hours. Be sure that the blood supply to the limb is intact and adequate before applying plaster. There may be little fever for a few days after plaster, or replaster, but this need not give rise to anxiety. The only indications for urgently removing a plaster are general malaise, a rising pulse, pain in the wound, oedema distal to the plaster with fever. It is not uncommon to find that the drainage of the wound has been inadequate, when the plaster has been removed for these symptoms. The immobilization in plaster stops absorption of toxins from the wound through the lymphatics, it protects the granulation tissue and the new epithelium from drainage and it stops secondary infection.

Late wounds, after removal of dead tissue, were packed lightly and splinted, and dressings were done infrequently, in many cases about 3 to 4 days. X-rays were available for us to locate foreign bodies, but a search for metal or glass in a wound at operation is unnecessary as the wounds heal quite well so long as dirt, clothing and rubble are removed. Sometimes these metal and glass fragments appeared in an abscess some 7 to 10 days later, and could be easily drained.

*Gas gangrene.*—Excision of a wound can prevent gas gangrene. This is a complication of war wounds, with *Clostridium welchii* as the main infecting organism. This organism is present in many wounds soon after injury and, according to Mullaly, it may give rise to (a) gas infection of the subcutaneous tissues or (b) true gas

gangrene. All wool clothing harbours gas-forming organisms, so that in London we were wary of it. The incidence of infection was up to 2.7 per cent. It is a more common complication in wounds received in cultivated and agricultural areas, and in external rather than colon wounds. Necrotic debris-laden tissues after damage by high explosive missiles provide a good medium for its growth, while sepsis, and calcium debris enable the organism to gain a hold. Typically the infection is of rapid onset, often within 24 hours, usually within 48 hours, but it may occur up to any time within four days from the injury, though very rarely at a later period. Damaged muscle, especially in the buttocks, is a common site for gas gangrene, which attacks muscles singly or in groups.

(a) *Gas infection of a wound.*—A grey exudate appears in the wound in 12 hours or so, and gas bubbles are visible in, and crepitation can be felt around, the wound in 24 hours from the time of injury. If the wound is purulent, there may be little change observed. In the wound, necrotic material—green, black and diffident sloughs—may be seen, full of gas. The wound exudes a brownish discharge and a typical musty odour is evident near the wound. There are crepitations and swelling of the wound, but *there is neither pain nor tension*. In 48 hours' time, the discharge increases, and many pyogenic cocci can be found there. The granulations become pale and exuberant, and in 10 days' time a normal granulating wound is seen.

(b) *Gas gangrene.*—This is spreading gangrene of muscular tissue, with toxæmia, in which death occurs from toxæmia or pyæmia, if no treatment is done. True gas gangrene is very rare after 4 days. Within 48 hours usually, there is *pain in the wound*. Pain in a wound is usually due to a rising tension in the wound from hæmorrhage, an uncontrolled fracture or a gas gangrene infection. Not only the wound but the whole limb becomes swollen. A rapidly rising pulse, rocketing up 10 to 20 points every four hours, is characteristic. There is some fever, with definite, often striking, malaise. In the next 24 hours the pain may subside as the mass of muscle becomes gangrenous, and the excited chatter of an euphoric patient may become evident. This and a continually rising pulse show a poor prognosis. The patient becomes thirsty, vomiting repeatedly as the muddy pallor and jaundice forecast his decline. The injured limb is swollen, its pale skin mottled by brownish stains. There is papable gas (which must be distinguished from free blood in the tissues) which rapidly extends. If the limb is not tense from swollen infected muscle, this extension of palpable gas is probably subcutaneous only. Blisters appear on the brownish skin, and are often followed by gangrene of the skin. A rapid increase of the swelling and of the toxæmia precedes death. In connection with this true gas gangrene, it is well to note that: (1) lower limb muscle wounds more easily succumb to infection and give more serious clinical features; (2) a large open lacerated wound of the buttock is more likely to develop only a gas infection, not gas gangrene, while a small wound in the buttock, with a mass of disorganized muscle there, is very liable to develop gas gangrene unless it is freely drained; (3) tension of the inflamed muscle tissues develops more quickly in large muscle masses, such as the retroperitoneal and the buttock muscles; (4) damage or spasm of the main vessels of limbs such as the femoral, popliteal, posterior tibial or brachial artery invites earlier development of gas gangrene in lacerated wounds distally.

*Treatment.*—Muscles are held in compartments by muscle fascia surrounded by deep fascia. They are supplied by a single arterial branch, which supply can be impaired by direct injury or by swelling of the muscle, when the veins and then the artery of supply are occluded inside the fascia. Treatment therefore is:

Avoid retention of tissue products under deep fascia. The wound in fascia is the size of the missile, while both muscle and skin wound are larger. By a longitudinal skin incision, the deep fascia is exposed and incised adequately in a longitudinal or cruciate fashion.

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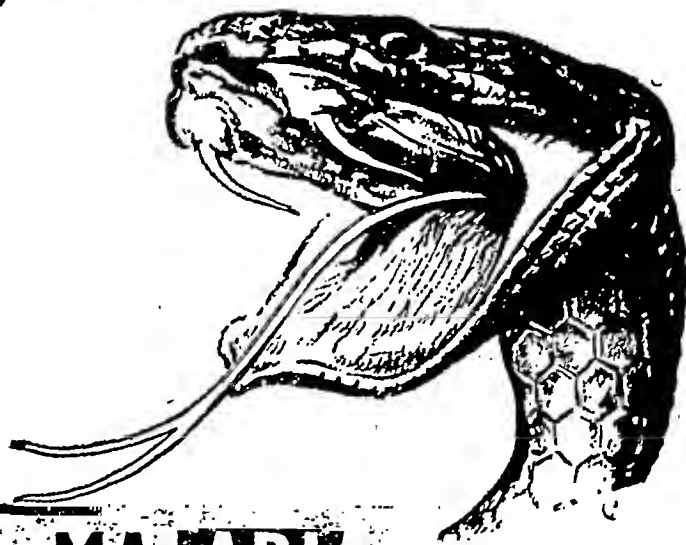
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Preserve the vascular and nerve supply to the muscle if possible. If only muscle groups are involved, these must be excised. If there is obvious spreading gangrene the limb must be amputated at a suitable level. The level of subcutaneous gas and its crepitus may have no relation to the level of the spreading infection in the muscles. Anti-gas gangrene serum and sulphanilamide are of value only in the treatment of gas gangrene, of uncertain worth in prophylaxis. X-ray therapy had results of variable nature and its worth in gas gangrene is as yet uncertain.

### BURNS

Burns from fires in buildings, from gas mains, from incendiary bombs were a special problem. Textbooks give six stages of burns but only three of these are of use clinically, as follows: (1) erythema, (2) vesication, and (3) skin and deeper destruction. The shock of burns causes much seeping of plasma into the burnt area, and resuscitation should employ plasma or serum to replace the lost fluid. All cases of burns received a cup of hot sweetened tea on admission. At least two pints of plasma were given if any serious shock was present; and to others one pint was given. If no recovery occurred after 2 to 3 pints, the outlook was hopeless. Morphine was given in small rather than large doses, only when pain developed (i.e. gr. 1/6 to an adult). Some cases of burn shock respond well to injections of desoxycorticosterone, but we saw very few cases treated by this. With adequate treatment, shock was usually well on the way to recovery in 6 hours. If recovery was delayed, treatment was less likely to be effective. In 24 hours, shock will either have killed the patient or will have been controlled by treatment. In 24 to 48 hours after injury, toxins from the burnt tissue having been absorbed into the circulation, a toxæmia may develop, resembling shock in the falling B.P. and rising pulse, but differing from shock in the time interval from the injury, slight pyrexia and slight jaundice being present. Intravenous glucose infusions help the liver to cope with the flood of toxins, and the toxæmia usually subsides. Sepsis may appear in the burn later and require local treatment. Burns of the face and front of chest are liable to be followed by pulmonary complications.

The treatment of burns is governed by three principles: Burns of certain sites and of a certain extent are a *danger to life*. Some others are liable to produce *much deformity*. The tannic acid treatment produced a 50 per cent drop in the general mortality from burns but in certain situations it produces much deformity. Therefore in large burns of the trunk, which may be mortal, a coagulant was applied. In burns of the hands, face, eyelids and flexures, which tend to produce deformity through sepsis, gangrene or scarring, a non-coagulant method was used. A non-coagulant method can of course be used for burns on the trunk, but we found that if these burns are 'tanned' for the first few days when life may be in danger, it proved to be best. The tan was removed for sepsis at times and then non-coagulative therapy only was continued. If the tan persisted without complication, it was left till it was cast off.

With this proviso, the following is the scheme we used for the treatment of burns:

*First degree burns.*—They need only sodium bicarbonate lotion; the 'leathery' feeling of the skin, especially in face burns of first degree, can be softened by rubbing in lanoline ointment.

*Second degree burns.*—As a first-aid measure, the application of sodium bicarbonate or saline lotion is useful. Tannic acid jelly applied to these burns, as a first-aid measure, is without serious consequences.

At hospital, under a general anaesthetic in the theatre, loose skin and blisters are removed from the burn edges, using saline swabs, rather than ether. A supple thin tan is made for the raw area with the following method of Atkins: Solutions of (i) 1 per cent gentian violet, (ii) 10 per cent tannic acid, (iii) 10 per

cent of silver nitrate are used, each solution being applied after the other, in this order, before the previous one has had time to dry. On the following days, the gentian violet solution is applied to any of the cracks and edges that appear; or weak tannic acid may be used. Sulphanilamide powder may be applied to the raw area before tanning, to prevent sepsis.

This method may be used on second degree burns on the limbs as well as on third degree burns of the trunk. If the burn is circumferential around the limb, the tan should be incised on each side of the limb to prevent its constriction producing distal oedema. In second degree burns of the hands, a saline compress, kept always sodden, applied over tulle gras or a single layer of vaseline gauze only was allowed. Cotton-wool vaseline pledgelets placed in the webs of the fingers prevented adhesion of the granulating surfaces there. The dressing is soaked off in 2 to 4 days, and a fresh granulating surface appears. For burns of the eyes, sodium bicarbonate lotion irrigation, followed by the application of vaseline on a glass rod, was used.

*Third degree burns.*—A 'wet' method, non-coagulating, was employed, especially in limb burns. A continually sodden saline compress on tulle gras dressing, with frequent changes of saline, was best for these burns. A 'triple dye' tan, as recommended by Wakely, was also used with success for both second and third degree burns, except that this type of tan needed frequent replenishment. A second degree burn, treated by 'tanning' at first, sometimes developed pus underneath the tan. The tan was then removed, and the raw area then treated by a wet method, as for third degree burns.

Third degree and septic burns were treated very successfully in saline and electrolytic hypochlorite solutions, by means of slipper baths for trunk burns, and a Bunyan bag for limb burns. [A Bunyan bag is a cellophane bag shaped to enclose an arm or leg, through which electrolytic hypochlorite solutions (e.g. 'Milton') are irrigated for certain periods each day.]

The raw areas from burns should be grafted as soon as possible with suitable Thiersch or pedicle skin grafts. As soon as the granulations are flat and of a healthy pink colour, and examination shows the absence of *B. pyocyaneus* (a potent cause of the failure of skin grafts), the time is ripe for skin grafting. A weak acetic acid lotion will remove *B. pyocyaneus*, and some sulphanilamide powder will deal with any other pyogenic organisms still thriving in the granulation tissue.

### ABDOMINAL INJURIES

These cases carry a mortality of 50 per cent or more, especially if over 8 hours have elapsed from the time of injury. Skilled and rapid surgery is essential. The sites of entry for missiles were 40 per cent anteriorly, 20 per cent posteriorly and 20 per cent via the buttock. The ease with which an entry wound in the buttock could be missed surprised us on many occasions.

I well remember one man, a policeman or an air raid warden I think he was, who had a buttock wound. He had come to hospital along with some twenty or thirty casualties and helped us in the sorting and distributing them to the appropriate hospital wards. As we finished dealing with the patients, he approached the receiving room officer for 'just a dab of iodine for a scratch on my buttock'. Luckily the senior surgeon was passing and heard the remark at the time. The man had, apparently, had the wound some 8 to 10 hours, but had been busy with rescuing these casualties, and had noticed no symptoms. The senior surgeon insisted on his admission for urgent operation. Within twenty minutes, we found that the tiny bomb splinter, which had penetrated the buttock, had lacerated the small intestine in six places and the large intestine in two places. He died from peritonitis and ileus a few days later. This case emphasized to us that the clothes of casualties must be removed as

soon as possible in order to allow a full examination, and that suspicious splinter holes need a full investigation.

It has been said, and I think we can confirm it, that in *seriously* shocked cases of penetrating abdominal wounds, there is usually a largish vessel in the mesentery bleeding. To delay anaesthesia in a case of an abdominal wound hoping that shock will improve, is usually a form of wishful thinking. The vital centres are damaged early, and unless bleeding is stopped soon, the resuscitation will never catch up. Haemorrhage is the most important factor in cases of abdominal wound with shock. A patient whose bowel only has been severed by a stab wound looks quite fit; a man with an intact abdominal wall over a lacerated piece of gut without any vessel damage shows few real signs in B.P. or pulse rate for several hours and has no symptoms for at least 2 hours. *It is very important that abdominal injuries should be submitted to early operation, even though they are suffering from shock.*

Local anaesthesia of the abdominal wall is quite satisfactory in these cases. The Russian surgeons, I hear, maintain that infiltration of the mesentery to its base with 0.25 per cent procain is usually effective in relieving any shock from gut injury alone. A dose of up to 15 grains of sulphanilamide powder is *most valuable* as a prophylactic for peritonitis. Large abdominal wounds with evisceration of bowel, often lacerated, have a very poor outlook and usually die.

*Head injuries.*—These cases were treated in much the same way as the ordinary peace-time head injury. When a head wound was explored, the discovery of an intact dura usually meant that damage to the underlying brain was small. Even so, at times we found a haematoma subdurally. Closed depressed fractures need the depression elevating as soon as any shock has passed off. Any tear in the dura must be repaired. Those cases showing a large skull defect and unconsciousness, or an open injury and *deepening* coma, or those with discharge of brain matter through the wound, a feeble pulse, unconscious fumbling with the external genitals are of hopeless prognosis.

As a first-aid measure in open head and scalp wounds, proper cleaning, excision and suture of the scalp within 10 hours will prevent secondary infection of C.S.F. or brain tissue or leakage of cerebrospinal fluid; fractures and foreign bodies in the brain can be dealt with later, so long as an adequate skin barrier has been set up to prevent secondary infection of the open wound. Epilepsy is commonest after septic head wounds, twice as common if the dura is penetrated than if it is intact, and begins usually within two weeks of the injury, but it may occur any time within the next 20 years. If the epilepsy began within two weeks of injury it is easily controlled, but the disease is never satisfactorily controlled if the onset of the epilepsy occurred any time after two years.

#### CONCLUSION

This, then, is part of the experience of many medical officers in the 'Blitz'. I have tried to tell you a little of the work and problems that we faced, of some of the advances in medical knowledge and practice which were made in the tragic experience of the months from September 1940 to May 1941. I hope that this experience may now be just past history for London, and that some of the things I have mentioned may be of value to you in your several medical practices. Most of the authorities from whose original papers much of our practice in London was built up, are impossible for me to trace. If I have trespassed unduly, I ask their indulgence.

### Estimation of Quinine in Urine

By A. J. GLAZKO

(Abstracted from the *United States Naval Medical Bulletin*, Vol. 41, March 1943, p. 529)

A SIMPLE technique for the estimation of quinine in urine is desirable as a means of checking on the

daily prophylactic use of the drug in malarious regions. An extensive survey of existing methods was made with the idea of establishing a reliable test for this purpose, suitable for use in the field. In the course of this work a quantitative method for the determination of quinine was also developed.

At least three general methods for the detection of quinine are available, depending upon: First, the well-known fluorescence of quinine in acid solution; second, the formation of coloured derivatives from oxidation products of quinine, of which the best known is the thallicoquin test; and, third, the formation of insoluble products with a large number of alkaloid precipitants, such as silicotungstic acid, Mayer's reagent, and the hemaphysite reaction with iodine. Most of these methods are not satisfactory for use with urine unless the quinine is first extracted with ether or chloroform from an ammoniacal solution. However, satisfactory results can be obtained directly on urine, using the double iodide of mercury (HgI<sub>2</sub>.K<sub>2</sub>) as the precipitating agent. This reagent has been used for the detection of quinine by a number of investigators; but the method described here incorporates a number of improvements, making the reagent more sensitive and suitable for quantitative work.

#### REAGENTS

1. The *double-iodide* is prepared by adding an excess of mercury (30 grams to a solution of 22 grams of iodine and 30 grams of potassium iodide in 20 c.c. of distilled water. The mixture is shaken vigorously until most of the brown colour has disappeared (7 to 15 minutes); and then, while still yellow, the solution is cooled rapidly under a running tap. The solution should be a light green colour when cool. It is diluted to 400 c.c. with distilled water and then decanted from the residual mercury. This solution will keep indefinitely. The reagent can be obtained on the market in granular form as Nessler's salt, which is convenient for immediate use in acid solution.

2. *Sulphuric acid.*—One part of the c.p. acid in 3 parts of water.

3. *Combined reagent.*—Equal volumes of the acid and double iodide solutions are mixed before use each day, so that only a single reagent is required for the test.

#### SIMPLIFIED FIELD TEST

To 5 c.c. urine in a test tube add 5 drops of the acidic double-iodide reagent. In the presence of quinine and certain other einchona alkaloids, a milky opalescence develops which is proportional to the amount of alkaloid present. Turbidity standards can be set up for comparison as an index of the quinine concentration. For field purposes, the urine specimens from men who did not take their quinine the night before will show only a faint turbidity.

The presence of more than 5 mg. per cent albumin will give a flocculent precipitate with the reagent which is quite distinct from that due to quinine, while less than 5 mg. per cent albumin produces a faint turbidity which may be confused with small amounts of quinine. This test produces a heavy milky opalescence, different from that of albumin, in urine taken the morning after a prophylactic dose of quinine. The presence of albumin is readily confirmed by boiling; the quinine iodomercurate dissolves, leaving a clear solution, while the albumin precipitate remains unchanged. If doubt should exist as to the presence of quinine together with a heavy albuminous precipitate, the sample may be boiled and filtered while hot. The albumin is removed and the milky opalescence of quinine iodomercurate reappears in the filtrate on cooling.

### Air Raid Injuries

(From the *United States Naval Medical Bulletin*, Vol. 41, March 1943, p. 538)

THREE years of British experience with air raids have significantly modified earlier concepts regarding the field casualty services.

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Almost all raids occur at night; the victims are crushed under the debris of demolished buildings and are either dead or severely injured; less than a third are slightly injured and can be cared for at casualty stations; all the severely injured must go to a hospital; victims are invariably covered with dust and dirt which hang in the air for hours. The conditions under which the rescue workers encounter the injured beneath the structural debris, the darkness, and the dust which always fills the air, the large proportion of dead and severely injured, and the urgent need for immediate hospitalization make it impossible to apply most peace-time concepts of first aid.

Wounds are usually grossly contaminated and need only be covered with a shell dressing until the casualty reaches the hospital. Hemorrhage is usually controllable with a pressure dressing. The tourniquet is rarely employed. Burns are covered only with a sterile gauze until the casualty arrives at the hospital. Tannic-acid jelly as a first-aid dressing for burns has been discarded because of the dirt which invariably contaminates the burned surface, because the jelly deteriorates rapidly, and, lastly, because tannic acid ignites in the presence of phosphorus when applied to burns caused by the explosion of phosphorus-oil bombs.

Traction splints are not used. An exception is made if the casualty must be transported a long distance over country roads. All that is done is to place the fractured extremity gently in alignment, bind it with triangular bandages to the uninjured leg or to an improvised splint, or apply a Thomas splint if one is on hand. Movement of the fragments can also be minimized by snug application of the blankets according to the Wanstead technique of blanketing and by the use of sand bags, which should always be carried in the ambulance.

Shock is treated at the incident by prompt administration of adequate doses of morphine (up to  $\frac{1}{2}$  grain for adults), coramine, proper blanketing, administration of fluids, and the use of hot water bottles during transportation to the hospital. The use of plasma or blood transfusion is deferred until arrival at the hospital; it is ordinarily quite impossible in the darkness, dirt, and confusion at the incident. (*Excerpts from Circular Letter of Dr. George Baehr to Regional Medical Officers, 10th November, 1942.*)

### Night Blindness, Improvement with Vitamin D

#### Including the Experimental Production of Retinitis Pigmentosa and its Treatment in Humans with Vitamin D.

By A. A. KNAPP

(Abstracted from the *United States Naval Medical Bulletin*, Vol. 41, March 1943, p. 373)

NIGHT blindness in the human may be caused by vitamin-D deficiency. Where this is so, the administration of vitamin D and calcium in sufficient dosage may remove this defect to a considerable degree.

Toxicity of these preparations, in the doses used, is negligible. In the light of our present knowledge the prescribed amount of vitamin D is small. The calcium dosage utilized is within physiological limits.

Retinitis pigmentosa—a comparable condition to that of humans—has been produced in dogs.

In the human, vitamin D and calcium have proved of value in treatment of this primary pathology of the retina. These night-blind patients were improved considerably. They were better able to see in the dark. In some cases the characteristic apple-jelly pallor of the optic nerve for a time changed to a normal pink or erythematous disc.

The night blindness of myopes often may be helped by prescribing these medications. Reduction of myopia was found in almost one-third of this series.

Night blindness may be caused by a deficiency of at least two vitamins—A and D.

Where it is desirable to improve the night vision of the patient, particularly in the armed forces, it would be well to fortify the diet with comparatively large doses of vitamins A and D.

### Lesions in the Tissues of the Body Following Sulphonamide Therapy

By H. J. SCHATTENBERG, M.S., M.D., F.A.C.P.  
and

W. H. HARRIS, Jr., B.A., M.D.

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXVIII, March 1943, p. 671)

A STUDY of a large series of cases and a careful review of the literature reveal the important finding that any organ or tissue in the body may be affected through the toxic action of the sulphonamides. In what percentage of cases this occurs is impossible to say. Considering the popularity of these drugs and the tremendous quantity used, amounting to over one-half million pounds of sulphanilamide for 1940 alone, it is not surprising to note some bad effects and even deaths from time to time.

The immediate effect of these drugs upon the skin, liver, kidneys, and nervous system is well understood. It is not possible at this time to say what residual effects may be noted in the myocardium, liver, or other organs years later. Might such changes lead to chronic myocarditis or cirrhosis of the liver? Might they lead to bizarre blood dyscrasia? No one as yet knows the answer.

Greater precaution in the use of these drugs is advisable. Dispensing on physicians' prescriptions only would lead to proper control and discourage abuse and indiscriminate use by the laity. It is certainly not the intent to discourage a drug which has proved its merit. At times, as in grave pneumonias, meningitis, puerperal infections, and otherwise serious bacteriæmias it may truly be a 'life-saver'. In cases of less gravity or in disease entities in which other therapy may be employed its usefulness is doubtful.

When sulphonamide therapy is indicated and necessary, certain precautions should be observed which may prevent disastrous effects from the toxicity of the drug. The amount of drug and duration of administration should be kept at a minimum consistent with beneficial results.

Frequent checking to determine proper concentration of the drug in the blood is essential. Frequent erythrocyte and leucocyte counts and hæmoglobin determinations with an immediate discontinuance of medication when there is evidence of important changes in these elements. An evaluation of renal function is necessary because a damaged kidney handles these drugs poorly. Progressive oliguria and hematuria may make continued administration of the drug hazardous. A continued high temperature after other signs of infection have disappeared may be entirely due to the drug. In a number of such cases observed the temperature has dropped to normal following the discontinuance of the sulphonamides. Alkalinization may prevent renal calculus formation. Electrocardiographic tracings may shed light on early myocardial changes following the use of these drugs.

An agent which is toxic for bacteria may in many instances be equally as toxic for the cells of the host and thereby increase the burden rather than lessen it. The normal tissues of the control animal, employed by the pharmaceutical firms, are affected to a lesser extent than the tissues and organs of a sick patient already the seat of cloudy swelling, fatty degeneration, etc., the result of bacterial toxæmia.

Undoubtedly, with a check on the injudicious use of the sulphonamides their discontinuance in diseases wherein the mortality is nil and where other forms of therapy are effective and close observation of the patient in whom their use is thought to be of decided benefit will result in fewer serious reactions and possible death.



## Emergency Vein

By M. E. PHELPS, M.D.

(From the *Southern Medical Journal*, Vol. XXXV, December 1942, p. 1091)

INTRAVENOUS medication is frequently a life-saving procedure. A venepuncture in the average individual is performed easily and safely providing a few basic precautions are observed. However, all physicians at times are confronted with an emergency where this procedure is difficult or impossible. These instances are probably encountered more frequently in treating the casualties of war both on the battlefield and in the civilian population which may be subjected to bombings, fires and other disasters that are concomitant with war.

Since the casualties on the battlefield are all male patients, intravenous medication or infusions can, if necessary, be administered through the corpus cavernosum of the penis. The availability of this puncture site is not generally recognized among the profession, although it is frequently a life-saving procedure.

Shaw in the *Journal of the American Medical Association*, 11th February, 1928, first described this procedure. Strain in the *Lancet*, 10th January of this year, again mentions its possibilities.

The technique is essentially as follows: a site is selected over the corpus cavernosum. While holding the penis firmly, the needle is inserted obliquely through the skin, the fascia (Buck's fascia) into the corpus cavernosum which is composed of venous spaces. The point of the needle should be directed toward the base. Ordinarily blood cannot be aspirated when the needle is in place. With a little care there is no danger of puncturing the urethra or the dorsal vessels of the penis. Slightly more pressure is needed for the injection than in the ordinary intravenous infusions due to the resistance of the fibromuscular tissue, but the rate of flow of the injection may be as rapid as is safe in other intravenous routes. Irritating solutions should not be used because of the risk of a chronic cavernositis, but this method is ideal for both blood plasma and citrated blood.

Following are cases in which this method was life saving.

**Case 1.**—In 1930, I was called to see a rather obese individual who had had a tonsillectomy 12 hours earlier. Following this, he had continued to bleed although he had been returned to the operating room two times and attempts had been made to control the hæmorrhage. A donor was obtained, but repeated attempts at venepuncture failed because of a collapse of the circulation. As a last resort the needle was inserted into the corpus cavernosum and 500 c.c. of citrated blood was given by the gravity method. Following this the bleeding stopped and the patient recovered.

**Case 2.**—A 12-day-old baby was brought to the hospital with tetanus neonatorum. It was in a state of almost constant tonic convulsions and very cyanotic due to the spasm of the respiratory muscles. We were unable to puncture a vein even after giving the child the usual sedatives. The corpus cavernosum was punctured and 20,000 units of anti-tetanus serum was administered in this manner, with subsequent recovery.

**Case 3.**—A 13-year-old boy was brought to the hospital following a gasoline explosion. He had suffered extensive burns on the face, neck, both arms and both legs. Due to the burns we were unable to find a vein and on three occasions blood plasma was administered through the corpus cavernosum of the penis without any apparent ill effect.

In none of the above instances did swelling of any consequence or any bleeding follow the puncture.

### Summary

The corpus cavernosum of the penis is an easily available site in the male patient for emergency transfusions of blood or blood plasma. Repeated punctures are possible.

This route is not recommended if the subcutaneous veins are accessible, nor is it recommended for any solution except blood plasma or citrated blood.

Although the field is limited, it is encouraging to know that there is always an 'available vein'.

This should be especially valuable in the emergency treatment of wartime injuries, as it could be safely done by a trained assistant on the battlefield.

## The Recognition of Virus-Type Pneumonia

(From the *Medical Press and Circular*, Vol. CCLIX, 5th May, 1943, p. 274)

RECENTLY 'atypical pneumonia' has been given a good deal of prominence in medical literature. It has been described as acute diffuse bronchiolitis, acute interstitial pneumonitis, acute pneumonitis, disseminated focal pneumonia, benign broncho-pulmonary inflammation, and otherwise. In most communications there is no direct evidence of virus causation, but the clinical pictures suggest it and certain features such as infectivity, length of incubation period, and the course of the disease agree closely with reported cases of atypical non-bacterial pneumonia in which a virus has been incriminated.

Confronted with such a medley of names and with such a number of distinctions without differences, the practitioner will be grateful to the authors who now offer him a solution of the riddle.

They hold that this non-bacterial atypical pneumonia should be named virus-type pneumonia and that virus-type pneumonia presents specific clinical features permitting diagnosis by positive findings. Diagnosis by exclusion is seldom necessary. On the basis of their own experience of fifty-two selected consecutive cases of this disease the authors present the following clinical account. The average incubation period is eighteen days. There is an insidious onset characterized by headache, cough and chilliness, with a muco-purulent sputum and some aching pain in the chest. Temperature and pulse disproportion and fever of considerable degree are also characteristic. The temperature has a sharply fluctuating course and falls by lysis. Generally the *alæ nasi* do not dilate and for the first four to five days there is no cyanosis. Even on the third and fourth day chest findings are insignificant in proportion to the degree of fever and are usually no more than a few râles with late inspiration, or a suppression of breath sounds. Initial chest roentgenograms are often not abnormal. Later, as more chest findings appear, roentgenograms may reveal infiltration. This is often lobular and bilateral; it may be lobar, it may be miliary, it may be unilateral or it may be migratory. The roentgenograms may closely resemble those of acute exudative tuberculosis unless this disease is differentiated by serial radiograms. In doubtful cases a trial of treatment with the sulphonamides may help to exclude a diagnosis of bacterial pneumonia.

Treatment is symptomatic. Only four deaths have so far been reported in the literature, but there is evidence that virus-type pneumonia is becoming commoner and that the virus, or viruses, are increasing in virulence. The disease, curiously enough, appears to increase the patient's resistance to secondary infection with pyogenic micro-organisms.

## Prescribing of Barbiturates.

(From the *Prescriber*, Vol. XXXVII, July 1943, p. 89)

DR. B. L. STANTON (*The Med. J. of Australia*) points out that the prescribing of soluble barbiturates in mixtures with such drugs as the bromides and chloral hydrate or even with tonic syrups is a common practice, but it is not one to be recommended. The soluble barbiturates are subject to hydrolysis, liberating their insoluble forms in acid solution, but in the absence of acid they form a strongly alkaline solution which will convert chloral hydrate to chloroform, will liberate

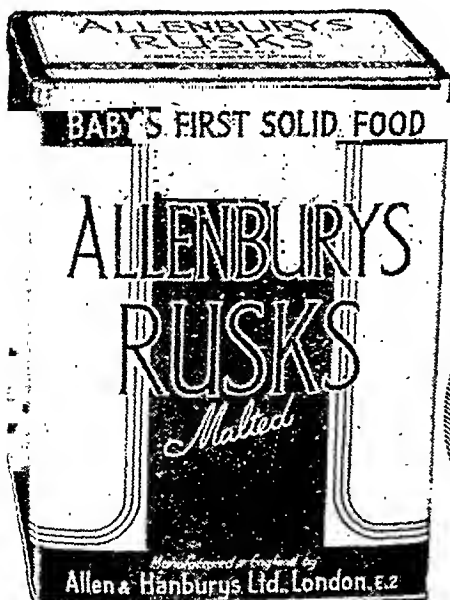
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ammonia from ammonium bromide, and may even precipitate any alkaloids in solution. It is much safer, therefore, for the prescriber, unless he is absolutely sure of his ground, to prescribe such complex remedies as the barbiturates by themselves.

## Reviews

**AFTER EFFECTS OF BRAIN INJURIES IN WAR. THEIR EVALUATION AND TREATMENT—THE APPLICATION OF PSYCHOLOGIC METHODS IN THE CLINIC.**—By Kurt Goldstein, M.D. 1943. William Heinemann (Medical Books) Limited, London. Pp. 244. Illustrated. Price, 21s.

THIS book is a detailed and careful analysis of cases of cerebral injury, collected mostly from last war material. Its particular value at this time is in its appreciation of the remote prognosis of cerebral injuries.

A careful psychological study forms a large part of the book and the degree of confirmation of present war casualties with the author's findings, remains to be established.

This is a useful and detailed work, and if the view tends to be backward in time, a number of good highways are marked out for future exploration.

H. P. J.

**PHYSIOLOGICAL PRINCIPLES IN TREATMENT.**—By Sir Walter Langdon-Brown, M.A., M.D. (Cantab.), Hon. D.Sc. (Oxon.), F.R.C.P., and Reginald Hilton, M.A., M.D. (Cantab.), F.R.C.P. Eighth Edition. 1943. Baillière, Tindall and Cox, London. Pp. viii plus 323. Price, 12s. 6d.

THE book has been thoroughly revised and brought up to date, and an entirely new chapter has been added on the action of drugs. It is pleasantly written, the reader being guided from a consideration of physiological principles to treatment. It does not aim at being a complete treatise on applied physiology but deals with certain selected subjects the knowledge of which will be of practical help to practitioners and senior students. It is an essentially clinical book, avoiding experimental work and laying emphasis on treatment. That it serves a useful purpose is evident from its long life of 34 years during which it has passed through eight editions.

R. N. C.

**WHITLA'S PHARMACY, MATERIA MEDICA AND THERAPEUTICS.** Fourteenth Edition revised by J. H. Burn, M.D., F.R.S., and E. R. Withell, B.Sc., B.Pharm., Ph.C., A.I.C. With the chapter on The Use of Vitamins in Medicine. By H. M. Sinclair, D.M. 1943. Baillière, Tindall and Cox, London. Pp. viii plus 525. Illustrated. Price, 14s.

THE book is divided into three sections—Therapeutics, Pharmacy and Materia Medica. As the authors rightly say, the number of substances used in medicine is now so large that an attempt to describe all within the pages of a small book is no longer possible. The section on therapeutics has consequently been modified, and briefly deals with those aspects of pharmacology which have an application in therapeutics. This section contains much information which will be of value to practitioners as well as students, stress being laid on the action of specific remedies in the body. Recent advances in the sulphonamides and vitamins have been included, and there is sufficient information about the action of the hormones. The section on pharmacy is very practical, and it is to be hoped that students will not neglect the instructions given therein. It is gratifying that the size of the book has been kept within reasonable limits.

R. N. C.

## Abstracts from Reports

### ANNUAL REPORT OF THE PREMANANDA FREE CHARITABLE OUT-DOOR DISPENSARIES IN CALCUTTA FOR THE YEAR 1942

THE war has affected the activities of these dispensaries in various ways. Scarcity of drugs and materials and abnormal rise in prices have increased the working expenses while dearness allowances have been granted to all the staff thus causing a good deal of anxiety with regard to the present financial situation. The Secretary, therefore, solicits public subscriptions for increasing income.

Owing to air raids in Calcutta during the last few weeks of the year there was a marked falling off in the number of patients attending the dispensaries. There were 680 new patients (Manicktolla 507 and Kalighat 173), last year's new cases at both clinics being 1,144. The total number of old cases was 1,173. Besides 360 beggars attended the dispensaries. Altogether they put in 47,570 attendances. They received anti-leprosy injections, general treatment and special treatment for malaria, dysentery and venereal diseases. The average daily attendances were 131.4 at Manicktolla and 93.4 at Kalighat; last year's figures were 162.8 and 105 respectively.

Of these patients 1,048 at Manicktolla and 474 at Kalighat attended sufficiently regularly to justify re-examination at the end of the year. The results were obtained:—

	Manicktolla	Kalighat
Disease arrested	55	44
Much improved	427	191
Slightly improved	344	185
Same as on admission	222	54

### THE THIRTEENTH ANNUAL REPORT OF THE ASSOCIATION FOR THE PREVENTION OF BLINDNESS, BENGAL, 1942-43

THE Association for the prevention of blindness, Bengal, was started in the year 1930, and since then it has worked hard and has been able to bring into existence five travelling eye dispensaries of which four are maintained by the Government of Bengal and the fifth by the Association itself. Besides carrying on propaganda work on the methods of prevention of blindness and its cure, by means of lectures, exhibitions of posters, magic lantern slides and films and free issue of pamphlets, etc., these dispensaries treated 60,532 cases in the mofussil during 1942-43. Many operations were also performed. A census taken in 115 villages showed the number of the blind as many as 155 per 100,000. The Association also runs an eye examination and lecture unit, the activities of which are mainly confined to Calcutta and its suburbs, its main object being to advise the public and particularly students how to take care of the eyes. Besides giving propaganda lectures and training health visitors from Sir John Anderson Health School in the care of eyes and prevention of blindness, this unit carried out eye examinations on 2,260 students of whom 34 per cent were found to have eye defects, the commonest being errors of refraction. Other activities include an investigation, with the help of a grant from the Indian Research Fund Association, of nutrition and its bearing on preventable blindness and eye diseases in Bengal. This has been carried out at the Eye Infirmary, Medical College, Calcutta, in collaboration with the staff of the travelling dispensaries. The final report will be published shortly, a proposal for trachoma research is now under consideration.

The thirteenth annual report of the Association which is now before us gives an account of its latest activities. Its financial position is satisfactory. We

have nothing but praise for the good work it is doing, and it deserves continuous support from the Government as well as the public.

#### REPORT OF THE COMMITTEE OF CONTROL FOR THE ROSS INSTITUTE OF TROPICAL HYGIENE, INDIA BRANCH, CALCUTTA, FOR THE YEAR ENDED 31ST JULY, 1943

THE report for the year ended 31st July, 1943, includes a survey of anti-malarial measures which the work of the Institute has established to be most effective and practical. As a result of infectivity surveys

in Assam and Northern Bengal, approximately 97 per cent of the infections were found in only one species, viz, *Anopheles minimus*, and a study of the breeding habits of this species provides the appropriate measures for controlling or eradicating it. These measures, both temporary and permanent, are briefly described and should prove interesting to those concerned in the control of malaria. Shortage of larvicides, insecticides and quinine has brought out the great importance of biological control measures of malaria such as flushing and shading. Control is better effected by a combination of different methods. The report pays a well-deserved tribute to the work of Dr. Ramsay, the Principal of the India Branch, and his associates.

## Correspondence

### A CRITICAL EXAMINATION OF THE DATE OF THE FIRST AUTHENTIC RECORD OF CATARACT OPERATION

SIR,—Certain observations seem to be warranted on some of the statements in the course of an article on 'Cataract operations in the pre-historic period' by K. C. Dutt of India, in July 1938 issue of the *Archives of Ophthalmology*. It is not the intention of this note to question India's claim for the priority of eye operations or to criticize the faults in translation of the long passages from Sushruta and Vagblata.

The writer of the article gives 1000 B.C. as the date of 'the first authentic record of an operation for cataract'. Any medical historian worth the name will rub his eyes and wonder whether any new inscription or papyrus or any clay tablet has been unearthed in India recently and is still unknown to the rest of the world. It may therefore be stated definitely and authoritatively that nothing of the kind has been discovered to justify the statement that the first authentic record of an operation for cataract can be traced to about 1000 B.C.

The author next proceeds to give the authority for his statement 'This record has been handed down in complete form in the *Sushruta Samhita*, which is a treatise on surgery, written by Sushruta, a great surgeon of ancient India. It has been ascertained that Sushruta practised and taught his method for the surgical treatment of cataract some time between 750 and 1500 B.C. As there is a difference of opinion as to the exact date that Sushruta first performed his operation, I may be excused if I agree with those historians who put it about 1000 B.C.'

This passage may pass as a current coin in medical circles ignorant of either scientific medical history or Indian history, just as any copper or silver piece counterfeit or damaged, and therefore unacceptable to civilized communities, may be grabbed and treasured by the primitive hill tribes who have never known currency and civilization. One would like to know—and if possible collect the replies of all the leading medical historians as well as the historians of Indian literature—how, when and by whom 'it has been ascertained that Sushruta practised and taught between 750 and 1500 B.C.'

A perusal of all the available treatises in English, German and French will promptly prove how erroneous the above assumption is. It is possible that some of the European scholars have been hypercritical in allotting a date to Sushruta. One writer has gone to the extent of asserting that Sushruta belongs to the ninth or tenth century A.D., building his theory on the supposed existence of a *Dhanvantari* in the Court of one of the many kings of India, who bore the name of Vikramaditya. At the other extreme, there are a

few Indian scholars who believe that Sushruta belongs to the age before the advent of Buddhism. The Ayurvedic pandits push the date back into 'Treta yuga'. The majority of medical historians such as Garrison, Neuburger and Oriental scholars such as Hoernle, Jolly and P. Cordier, etc., allot Sushruta to an age ranging from one or two centuries before Christ to the first century after Christ. Most of the authorities also accept the view that the *Samhita* was redacted and supplemented by the great Buddhist divine and the founder of Mahayana, Bodhisatva Nagarjuna. This great scholar, rightly called the 'Aristotle of Buddhist India', is, by competent authorities, declared to have lived about the close of the first century or in the early part of the second century A.D.

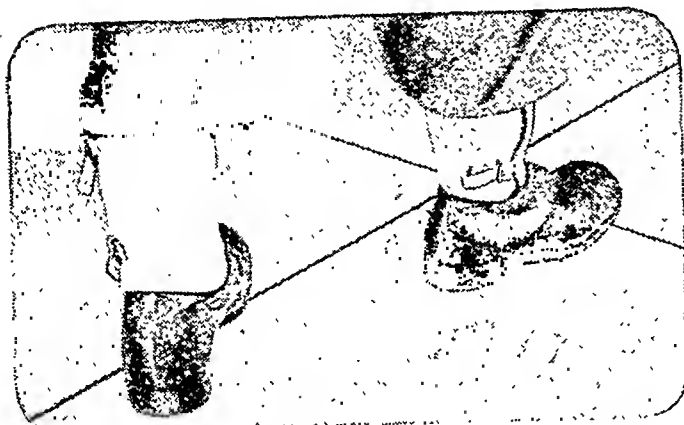
The Bower manuscript, assigned to the fourth century A.D., and unearthed in Eastern Turkistan and edited and published by Dr. Hoernle of Oxford, contains some extracts and prescriptions from Sushruta, and this is the most undeniable and indisputable proof we have, so far, regarding the latest limit to the age of the *Sushruta Samhita*.

The *Charaka Samhita* is regarded as a more ancient treatise in Ayurvedic tradition. Even if it is contended that it is the original *Agnivesa Samhita* that is regarded as the earlier of the two great Ayurvedic treatises of ancient India, the evidence for any assumption that Agnivesa flourished between 750 and 1500 B.C. is either utterly lacking or has no foundation in material facts. Whether the age of composition of the earliest *Samhitas* usually regarded as commencing from 600 B.C. can be pushed back to 1500 B.C. or even 1000 B.C. is a matter on which Sanskrit scholars and Orientalists are competent to express any opinion. The archaeologists need also to marshal evidences whether or not Takshasila and Benares were centres of such advanced learning, indicated in these *Samhitas*, at the early period of 1000 B.C.

The contention of the writer of this note is that scientific medical history, as distinguished from uncritical repetition of legends, fables or a craze for hoary antiquity, cannot accept any dogmatic statements about the age of Sushruta, without clear and impeachable proof, acceptable to archaeologists, medical historians and Sanskrit scholars of international standing. It may be said that there is no harm in expressing an opinion or agreeing with the minority view held by one or two Indian scholars, who may not be known to the world or even to India. More than the erroneous information thus broadcast, the method of presenting and the manner of assuming and asserting certain statements unsupported by adequate evidences or authorities or data require correction and also a certain amount of gentle admonition.

E.D.6.

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The date of Vagbata also deserves a closer scrutiny than has been vouchsafed by the author. I refrain from giving the relevant references and authorities for want of space.

Finally it will be worth while to study the original text of Sushruta, particularly the earliest manuscripts available, side by side with the commentaries of Dallana and other medieval Ayurvedic scholars, to test and prove whether the description of the operation of cataract occurs in the portion attributed to Sushruta and not in Uttarasthana (supplement added by Nagarjuna) or the still later additions and interpolations.

The Journal which has published and created an interest in the earliest description of cataract operation by Sushruta would, one hopes, also keep a watchful eye, as a specialist journal of international fame that any unsupported statements or erroneous information

is not published as authoritative, without proper verification of facts and statements by competent scholars. No one would be more pleased or gratified than the writer of this critical note if it is proved that he is wrong and the statements in the above article are recognized as correct and unquestionable by any court of international scholars or medical historians.

D. V. S. REDDY.

Corresponding Member, American  
Association for History of  
Medicine.

ANDHRA MEDICAL  
COLLEGE,  
VIZAGAPATAM,  
15th October, 1943.

## Service Notes

### APPOINTMENTS AND TRANSFERS

COLONEL (LOCAL BRIGADIER) G. COVELL, C.I.E., V.H.S., resumed charge of his post of Director, Malaria Institute of India, with effect from the 21st September, 1943.

His Excellency the Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's personal staff, with effect from the 20th October, 1943 :—

*To be Surgeon to His Excellency the Viceroy*

Lieutenant-Colonel H. H. Elliot, C.I.E., M.B.E., M.C. Lieutenant-Colonel S. L. Bhatia, M.C., was appointed to officiate as Deputy Director-General, Indian Medical Service, from the afternoon of the 31st July, 1943, to the 3rd October, 1943, and to hold the post substantively, with effect from the 4th October, 1943, *vice* Major-General J. B. Hance, C.I.E., O.B.E., V.H.S.

Lieutenant-Colonel R. McRobert was appointed to officiate as Civil Surgeon, New Delhi, *vice* Lieutenant-Colonel Whyte, granted leave.

Major Jaswant Singh reverted to his post of Assistant Director, Malaria Institute of India, with effect from the 21st September, 1943.

On release from military duty Major C. F. Garfit assumed charge of the Office of Deputy Inspector-General of Civil Hospitals, Punjab, Lahore, on the forenoon of the 24th December, 1943.

Captain T. P. Binns is appointed as Medical Officer for the Kashgar Consulate-General and His Britannic Majesty's Acting Vice-Consul, Kashgar, with effect from the afternoon of the 23rd October, 1943.

#### INDIAN LAND FORCES

#### INDIAN MEDICAL SERVICE (Emergency Commission)

##### *To be Captain*

Gomatam Rachavachari. Dated 17th October, 1943.

#### SECONDED TO INDIAN MEDICAL CORPS

##### *To be Captains*

Byrappa Marisiddappa. Dated 7th July, 1943.  
Doddaballapur Krishnamurti. Dated 12th October, 1943.

Anni Singaravelu Venkatachalam. Dated 14th October, 1943.

Basaya Mallaya Pujari. Dated 15th October, 1943.

Sisir Kumar Chatterjee. Dated 14th October, 1943.

Kochappy Raghavan. Dated 16th October, 1943.

Jal Framroze Bhajiwalla. Dated 20th October, 1943.

The undermentioned officers are transferred to the General Cadre, with effect from the dates specified :—

#### INDIAN LAND FORCES

#### INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commission)

Captain R. C. Chakravarti. Dated 16th September, 1943.

Captain Santibrata Ghosh. Dated 20th September, 1943.

Captain Albert Jayme Ribeiro. Dated 1st October, 1943.

The undermentioned officer reverts from the Royal Indian Navy and is seconded to the I.A.M.C.

#### INDIAN LAND FORCES

#### INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commission)

Captain T. R. Seshadri. Dated 27th October, 1943.

The undermentioned officer of the Indian Medical Service reverts from the I.A.M.C. and is seconded for service with the Royal Indian Navy.

Captain M. G. Leane. Dated 1st October, 1943.

#### (WOMEN'S BRANCH)

##### *To be Captains*

(Miss) Zubaida Haji Yousof Sobani. Dated 20th September, 1943.

Mrs. Rose Swamikan. Dated 23rd October, 1943.

The undermentioned officers revert from the I.A.M.C. and are seconded for service with the Indian Air Force.

#### INDIAN LAND FORCE—INDIAN MEDICAL SERVICE (Emergency Commissions)

Captain H. N. Sen. Dated 31st July, 1943.

Captain B. S. Khangura. Dated 10th August, 1943.

Lieutenant H. P. Gnanaolivu. Dated 13th August, 1943.

Lieutenant M. K. Mukherjee. Dated 16th August, 1943.

Lieutenant L. D. Kale. Dated 18th August, 1943.

Lieutenant K. K. U. V. Raja. Dated 20th August, 1943.

Lieutenant M. S. Maini. Dated 23rd August, 1943.

28th September, 1943

Lieutenant D. Bhatia. Lieutenant H. S. Sethi.

Lieutenant V. B. Kalra. Lieutenant D. N. Gupta.

Captain N. Sen Gupta. Dated 14th October, 1943.

## LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN  
ARMY MEDICAL CORPS

## (Emergency Commissions)

## To be Lieutenants

(Mrs.) B. L. H. Sergeant. Dated 2nd June, 1943.  
Satyendra Nath Basu. Dated 15th October, 1943.  
Arthur Donald Stanislaus McLaughlin. Dated 16th  
October, 1943.

## PROMOTIONS

## Lieutenant-Colonels to be Colonels

K. S. Master, m.c. Dated 22nd August, 1943.  
N. Briggs. Dated 8th November, 1943.

## Major to be Lieutenant-Colonel

S. C. H. Worseldine. Dated 14th October, 1943.

## INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN  
ARMY MEDICAL CORPS

## (Emergency Commissions)

## Captains to be Majors

P. B. Kurup. Dated 15th November, 1943.  
R. Bhattacharya. Dated 23rd November, 1943.  
The undermentioned officers (on probation) are  
confirmed in the Indian Medical Service with effect  
from the dates specified :—

10th January, 1939

Captain J. E. Ennis. Captain H. R. Loughran.

12th March, 1939

Captain R. M. McCulloch. Captain H. V. Morris.  
lough. Captain F. W. Snedden.

27th September, 1939

Captain S. G. Nardell. Captain K. D. Fraser.  
Captain D. H. Harrison.

Captain L. E. Ellerton. Dated 28th April, 1939.

12th May, 1939

Captain A. M. Best. Captain J. Lightbody.  
Captain H. F. T. MacFetridge.

Captain P. M. Kirkwood. Dated 10th January, 1939.  
Captain W. D. P. Griggs. Dated 19th October, 1939.

## LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN  
ARMY MEDICAL CORPS

## (Emergency Commissions)

## Lieutenants to be Captains

28th May, 1941

W. H. S. St. John-Brooks. J. L. MacCallum.  
O. J. S. Macdonald. G. B. Bowater.  
G. C. Trevisder. C. Ibbotson.  
W. R. Smith. W. L. P. Spicer.  
M. Shaw. O. B. Breares.  
J. M. French. H. R. Carr.  
S. F. Seelig. E. Fletcher.

L. R. Flowers.

27th April, 1943

B. A. Barlow. L. M. Reeve.  
C. W. Bamford. Dated 5th April, 1943.  
K. P. Roe. Dated 15th June, 1943.  
P. R. Sondhi. Dated 13th July, 1943.  
S. K. Mitra. Dated 23rd September, 1943.  
T. V. Rao. Dated 17th October, 1943.  
P. B. Roy. Dated 20th October, 1943.  
C. M. Dave. Dated 18th August, 1943.  
M. Ismail. Dated 4th September, 1943.

1st October, 1943

K. C. Das Gupta. A. Das Gupta.

2nd October, 1943

G. N. Sen Gupta. R. K. Ghosh.  
S. K. Das.

S. K. Das. Dated 5th October, 1943.  
O. N. Tyagi. Dated 7th October, 1943.  
F. R. S. Kellett. Dated 9th October, 1943.

19th October, 1943

B. S. Dhillon. S. S. Harnal.  
Y. P. Lullah. J. Singh.  
M. I. D. Sharma.

20th October, 1943

N. K. Khanna. Z. U. Khan.  
V. P. Malhotra. C. M. S. Bajwa.  
G. D. Koshal. P. Singh.  
H. S. Qazi. J. S. Khoranna.  
M. M. Khan. B. A. Butt.  
A. H. Khan. Dated 2nd October, 1943.

23rd October, 1943

P. N. Chhabra. R. N. Banerjee.  
N. N. Banerjee. Dated 24th October, 1943.  
P. N. Bhattacharjee. Dated 25th October, 1943.  
B. N. Narula. Dated 27th October, 1943.  
M. S. A. Wasty. Dated 28th October, 1943.

30th October, 1943

M. V. Bapat. N. N. Das.  
S. C. Vij.

31st October, 1943

R. Gnanadorai. R. Krishna.

## RESIGNATION

## INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN  
ARMY MEDICAL CORPS

## (Emergency Commission)

Captain (Miss) V. V. Saberwal. Dated 18th May,  
1943.

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# Original Articles

## NOVARSENOBILLON AND MAPHARSIDE IN THE TREATMENT OF THE ATTACK OF MALARIA

By J. LOWE, M.D

Officiating Professor of Tropical Medicine, School of Tropical Medicine, Calcutta

ARSENIC in various forms has for many years been given in malaria, sometimes to patients suffering from malarial fever, but more often to those convalescing from malaria.

The use of arsenic after an attack of malaria is traditional. We have however traced no definite statement regarding the rationale of such a use of arsenic; it is apparently intended to combat the anæmia and to reduce the tendency to relapse, although there is no proof that it does so. This use of arsenic is not discussed any further here. The writer has had no opportunity of studying this matter or of assessing the value of arsenic used in this way. We are here concerned with the use of arsenic in the control of an attack of malaria.

The history of the use of arsenic in the attack of malaria really dates from the introduction of the arsphenamines. The earliest available reference to the subject in the literature is that of Werner (1910); and there are several other early contributions on the subject; altogether over twenty publications on the subject have been traced. Most of these publications appeared shortly before, during, and after the last war, when the subject raised considerable interest. Certain limitations of the treatment of malaria with these preparations then became apparent, and the subject was left there.

What brought the matter to life again was the introduction of malaria therapy for neuro-syphilis. Here one was dealing with a known species of the parasite, usually *P. vivax*, and the efficacy of the neoarsphenamines in the control of *P. vivax* infection was clearly indicated. Moreover the use of the neoarsphenamines was obviously not contra-indicated in persons suffering from neuro-syphilis. Therefore several publications appeared on this matter, and the neoarsphenamines came to hold a definite place in the control of therapeutic malaria, but no one suggested their use in naturally acquired malaria until Goldman (1938) described the cure of a case of naturally-acquired malaria with numerous relapses with the new trivalent arsenical preparation produced by Parke, Davis & Co., and known as mapharside\*. This preparation in syphilis is of high potency and low toxicity. Niven (1940) tested this preparation in naturally acquired malaria in Malaya against *P. falciparum*, *P. vivax* and *P. malariae*. Niven's

two tables summarizing the effect of the drug on the peripheral blood findings are here reproduced.

TABLE I

*Disappearance of asexual parasites in acute falciparum malaria treated with mapharside or quinine*

	Number of cases showing asexual parasites each day following commencement of treatment						
	1	2	3	4	5	6	7
Mapharside	18	17	18	18	18	18	18
Quinine ..	20	20	18	6	2	1	0

TABLE II

*Disappearance of asexual parasites in acute vivax malaria treated with mapharside or quinine*

	Number of cases showing asexual parasites each day following commencement of treatment						
	1	2	3	4	5	6	7
Mapharside	20	8	0	0	0	0	0
Quinine ..	20	20	13	5	1	0	0

His conclusions were as follows :—

Mapharside is found to have dramatically rapid effect on the sexual and asexual forms of *P. vivax*.

Mapharside is shown to be relatively inert against *P. falciparum* and *P. malariae* and to have little effect on either the production or the viability of 'crescents'.

It is concluded that the place of mapharside in the treatment of malaria is limited and will probably be mainly confined to therapeutic vivax malaria. The drug may possibly be of value also in chronic relapsing vivax malaria but on this point further evidence is desirable.

These findings are quite definite and clear-cut, and in normal times with adequate quinine available, no one would think of recommending these preparations for the treatment of naturally acquired malaria in general. In fact such a procedure will be fraught with danger and might cause many preventable deaths, for the dangerous form of malaria, namely *P. falciparum* infection, is little influenced by this treatment.

In times of quinine shortage, however, other considerations come into play, and it might be justifiable in suitable cases to make use of the anti-malarial properties of these arsenical preparations.

The work briefly reported in this paper was undertaken with the following objects: (1) To find out whether in patients in hospital in whom blood examination and the identification of the parasite were possible, the treatment with neoarsphenamines might reasonably be adopted. (2) To find out whether the new preparation mapharside was more effective in controlling malarial fever than the older preparations such as novarsenobillon.

Patients were admitted to hospital showing malarial fever and malarial parasites in considerable number in the blood. They were

\* Actually mapharside is not an arsphenamine but an arsenoxide.

kept without any treatment, if possible for two or three days, to make sure that the infection was not a naturally subsiding one. (This fact made it impossible to study heavy infections of malignant malaria, because it was considered dangerous to keep them without any treatment.) Treatment was then instituted, and the effect of the treatment on the fever and on the peripheral blood findings was carefully recorded by the keeping of 4-hourly temperature charts and by careful examination of blood films twice daily morning and evening. In some cases, parasite counts were also done, and in all cases the rough estimation of the number of parasites was made.

In all, about 20 cases were treated. It is not proposed here to present details of all the 20 cases but merely to outline the main findings.

(a) *Results in benign tertian malaria*

Novarsenobillon was given intravenously to begin with in doses of 0.15 gramme and later in doses of 0.3 and 0.45 gramme. To begin with only one injection was given, but later the number of injections was increased to three at intervals of 4 or 5 days.

On the whole, the results of treatment were excellent. A single injection of novarsenobillon cut short the attack of malaria very promptly. The temperature fell to normal within 24 hours, and the peripheral blood became negative usually within 48 hours, sometimes within 24 hours. Our findings agree with those of Goldman, that the effect of arsenic in benign tertian malaria is more dramatic than that of quinine. The patients suffered none of the discomforts usually associated with quinine treatment.

The treatment, however, had certain disadvantages which became clear. After one injection only, relapse was common, sometimes within a few days, and after two or three injections also, relapse was not infrequent but at a later period. It cannot be said that after three injections the relapse rate was higher than it is after a one week's course of quinine, but the relapse rate was sufficiently high to indicate that even after three injections the treatment failed to eliminate the infection in a considerable number of cases.

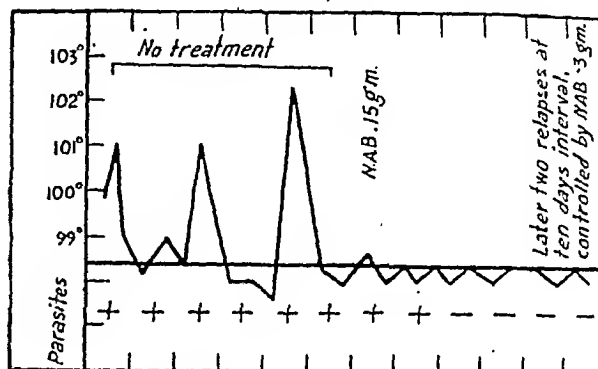
Another disadvantage of the treatment lay in the fact that even though a patient on admission showed only benign tertian parasites in the blood, there was in some cases a latent malignant infection which revealed itself only after the tertian parasites had disappeared as the result of treatment. This is another indication of the fact that *P. falciparum* is not susceptible to the action of arsenic.

With mapharside, results were similar to those obtained with novarsenobillon. The dose of mapharside given was 0.04 gramme. The number of patients treated with mapharside was not large, so final conclusions are not justifiable, but there was no definite evidence that mapharside was any more effective in controlling the fever and making the peripheral blood negative than novarsenobillon; in fact the evidence was

rather to the contrary; the results obtained with mapharside were not quite so dramatic as those obtained with novarsenobillon.

*NAB. in P. vivax infection.*

Fever controlled and blood made negative.  
Relapse



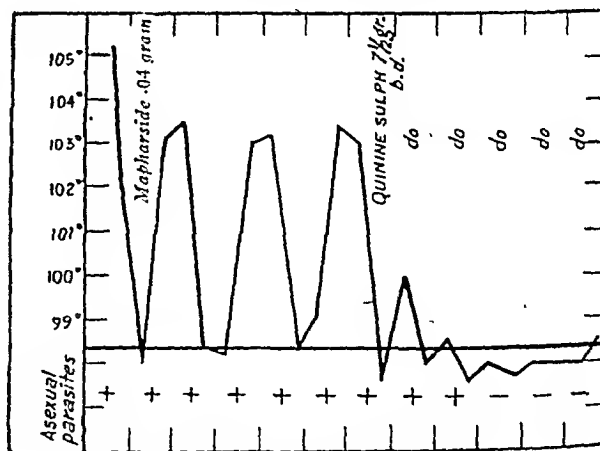
Results with MAPHARSIDE were similar.

(b) *Results in malignant tertian malaria*

In malignant malaria both mapharside and novarsenobillon had very little effect. The cases studied were all of low grade infection, with low fever, and *P. falciparum* constantly in the blood, but neither of the arsenical preparations used appeared to control the fever or to cause the disappearance of parasites from the blood. In all the cases, quinine treatment had to be instituted, and the response to treatment with quinine was excellent.

*MAPHARSIDE in P. falciparum infection.*

Failure: fever easily controlled by quinine.



Results with NAB. were similar

*Conclusions*

Though the number of cases treated was not great, it was not considered justifiable to continue this line of investigation further. The experiment indicated clearly that the use of these two arsenical preparations in the treatment of malaria had severe limitations. They could only be used with safety in cases in which one was quite sure that one was dealing with a pure *P. vivax* infection. Our experience in

(Concluded on opposite page)

## ORGANIC ARSENICALS IN THE TREATMENT OF SIMIAN MALARIA

By B. M. DAS GUPTA

and

L. B. SIDDONS

(From the Department of Protozoology, School of Tropical Medicine, Calcutta)

It appears from the literature that organic arsenical compounds, such as the salvarsans, have not given results which justify their employment in the general treatment of malaria : a certain measure of success has been reported only in tertian malaria (*P. vivax*). Recently, however, Goldman (1938) has claimed striking results with 'mapharsen' in the same type of malaria : among 24 cases treated with this drug only 2 relapsed, and these were among the group of 14 cases who received but one injection of 0.04 to 0.06 gm. of the drug. On the other hand, Young and McLendon (1939) found that mapharsen failed to eradicate the parasites in

(Continued from previous page)

Calcutta is that one can very rarely be sure of this. Even if one could feel sure, and applied the treatment with either of these preparations, the relapse rate would still be considerable. It is therefore clear that neither of these preparations can be recommended for wide use in the treatment of malarial fever.

It is, however, not impossible that a combined treatment of one of these preparations with quinine might be a very effective treatment for malaria, and that the relapse rate might be considerably reduced. We have no definite evidence on this point and are not at present in a position to study the matter. Nevertheless in *P. vivax* infection, the results of a single injection are usually so dramatic and the fever is so quickly controlled that the writer feels that if he himself developed an attack of malaria due to this parasite, he would feel strongly tempted to start his treatment with one injection of neoarsphenamine, and then to take quinine.

At the same time as the work was being done on human subjects mapharside was supplied to Dr. B. M. Das Gupta for trial in monkey malaria. His findings (reported elsewhere in this journal) are that in *P. knowlesi* infection in monkeys, mapharside has little therapeutic effect.

## Acknowledgment

I wish to acknowledge the free gift of the supply of mapharside for use in this work by Messrs. Parke, Davis & Co., Bombay.

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any one of 10 cases of induced quartan malaria (*P. malariae*), though the symptoms were relieved; the viability of the parasites was not affected. Recently Lowe at the School of Tropical Medicine has been experimenting with arsenicals in the treatment of human malaria, and, as an extension of this work, trials have been made with mapharside (the British name for mapharsen) and novarsenobillon ('N.A.B.') against *P. knowlesi*.

## Material and methods

The methods of inducing *P. knowlesi* infection in rhesus monkeys (*S. rhesus*) and of estimating the intensity of the infections have been described elsewhere (Das Gupta and Siddons, 1943). The strain of *P. knowlesi* maintained in this laboratory almost invariably produces typical infections of a progressive and fatal character in monkeys, but the infection can be controlled by an efficient anti-malarial drug. These facts, together with considerations of economy under the present abnormal war-time conditions, have led to the minimum use of control animals in investigations on anti-malarial drugs being conducted in the department.

'N.A.B.' and mapharside were given daily by intravenous injections. The quantity of 'N.A.B.' in an injection varied from 0.0075 gm., or one-twentieth of the human dose of 0.15 gm., for a monkey weighing 1½ kilos, to 0.1 gm., or one-third of the human dose of 0.30 gm., for a monkey weighing 2 kilos. The dosage of mapharside was 0.004 to 0.01 gm., from one-tenth to one-fourth of the human dose of 0.04 gm., for monkeys weighing 1½ to 3 kilos.

## Observations with 'N.A.B.'

The essential data are given under experiments numbered 1 to 6 in the table.

In experiments nos. 1 to 3, quantities of 0.0075 to 0.045 gm. of the drug gave little or no evidence of parasitocidal action, and the infections increased to fatal intensities. The dosage of 0.0045 gm. (experiment no. 3) had some effect on the parasites, for the infection rate of the red cells remained stationary at roughly 6.2 per cent from the fourth to the sixth day of treatment. The parasites then appeared to recover their vitality, and the infection rate rose to 16 per cent, after which the animal was treated with a more efficient anti-malarial drug and the infection was controlled.

With higher doses of 0.06 to 0.09 gm. (experiments nos. 4 and 5), the infections were incompletely controlled and the animals survived; parasites could be found in the peripheral blood for at least eleven days after commencement of treatment. In experiment no. 6, treatment with 0.1 gm. of the drug gave the kind of results expected of an effective anti-malarial agent, with appreciable evidence of direct action on the parasites, but it was not surprising that such a large dose could not be tolerated.



Therefore the administration of 'N.A.B.', while having some action, is not an efficient method of treatment of simian malaria due to *P. knowlesi*.

#### Observations with mapharside

The data for tests with this drug are shown under experiments nos. 7 to 14 in the table.

sporulated, with the result that the infection rate rose from 12.6 to 20 per cent.

In the remainder of the experiments, the infection rate of the red cells was always higher after the course of treatment than before, though usually after the first or second dose a temporary decrease could be noted for one or two

TABLE  
*The effect of arsenicals on simian malaria (P. knowlesi)*

Serial number of experiment	Animal number	Treatment, number of doses $\times$ quantity (gm.)	PERCENTAGE OF INFECTION OF R.B.C.		REMARKS
			Before treatment	After treatment	
(a) 'N.A.B.'					
1	27	$1 \times 0.0075$	17.0	?	Animal died morning after treatment; heart blood showed very heavy infection with normal parasites. Object of experiment was to test effect of drug on morphology of parasites. No effect observed.
2	30	$1 \times 0.015$	5.8	21.4	Further treatment with mepacrine hydrochloride failed to save the animal.
3	32	$2 \times 0.03$ $6 \times 0.045$	Below 0.1	16.0	Animal had to be treated with a more efficient anti-malarial.
4	34	$7 \times 0.06$	0.8	1.4	During treatment infection rate rose to 9.8 per cent, then decreased to chronic level. Blood became negative only after treatment with another anti-malarial. A small proportion of parasites showed degenerative changes.
5	40	$2 \times 0.075$ $5 \times 0.09$	13.2	Below 0.1	Parasites persisted for 11 days before further treatment with another drug terminated the infection.
6	42	$2 \times 0.1$ $1 \times 0.045$	10.4	Below 0.1	Infection reduced to chronic level, but animal died on the 4th day after commencement of treatment—dosage probably not tolerated.
(b) MAPHARSIDE					
7	44	$2 \times 0.004$	?	?	Shown heavy infection when treated; up to 5 per cent of parasites showed degenerative changes after treatment. Animal died.
8	49	$4 \times 0.004$	1.4	6.0	Animal died 2 days after last dose, heart blood showed parasites.
9	50	$5 \times 0.004$	0.4	18.2	Do.
10	51	$1 \times 0.008$	15.2	20.0	Treated when parasites were in the 'ring' stage; 20 hours later mostly normal schizonts present (infection rate 12.6 per cent). These were allowed to sporulate when rate became 20 per cent. Treatment with another drug did not save the animal.
11	54	$3 \times 0.008$	10.0	?	Animal died day after 3rd dose; heart blood showed moderate infection. After 2nd dose count was 12 per cent.
12	57	$4 \times 0.008$	0.2	35.0	Animal died day after last dose; heart blood showed 35 per cent infection rate. Control monkey treated with another drug when showing 14 per cent infection; infection controlled and animal still alive 2 months later.
13	63	$4 \times 0.01$	13.0	16.3	After 2 doses count was 8 per cent. Treatment with another drug failed to save animal. Untreated control died 2 days earlier.
14	65	$4 \times 0.01$	1.0	12.2	Treated with another drug; animal alive.

Experiment no. 7 was designed to facilitate the observation of the effects of the drug on the morphology of the parasites. The proportion of parasites showing such an effect was not greater than 5 per cent. In experiment no. 9, 0.008 gm. did not prevent the development of the parasites from 'rings' into normal mature schizonts which

days, after which the infection rate rose again to peak level. Animals not receiving further treatment with a more efficient drug died during the primary infection.

The conclusion is that mapharside has no significant action against *P. knowlesi*.

(Continued on opposite page)

# THE ACTION OF 2-CHLORO-7-METHOXY-5 (8-DIETHYL-AMINO-BUTYL) AMINO-ACRIDINE ON SIMIAN MALARIA

By L. B. SIDDON'S

and

A. N. BOSE

(From the School of Tropical Medicine, Calcutta)

In a previous paper it was observed by one of us (Basu and Bose, 1941) that although the toxicity (LD/50) of 2-chloro-7-methoxy-5 (8-diethyl-amino-butyl) amino-acridine, in mice, was only slightly higher than that of 2-chloro-7-methoxy-5 (8-diethyl-amino-iso-amyl) amino-acridine, the toxic effect of the former on cultures of *Paramecium caudatum* was found to be remarkably greater than that of the latter.

The toxicity of any compound on paramecia has been found to resemble closely its toxicity on other protozoal organisms (Kindler, 1938). The amyl-acridine derivative (under the trade name 'atebrin') is a well-known anti-malarial drug. Chopra and Das Gupta (1933) have demonstrated that this drug possesses a definite action against simian malaria. It was, therefore, considered to be of interest to investigate the action of the butyl-acridine, first, on *Plasmodium knowlesi* in the monkey, *Silenus rhesus*, and later, on the human plasmodia.

## Methods

The technique followed in the investigation was essentially that of Chopra and Das Gupta (1933), with the difference that the infection rate of the red blood cells was studied rather

than the parasite rate. The drug was administered by intramuscular injection in sterile watery solution. Sets of doses varying from 25 mg. to 5 mg. were tried with the object of ascertaining the effect of smaller doses. The drug was administered in mild and heavy infections. The monkeys used were of roughly the same size, and those that were weighed scaled about 2 kilos.

## Observations

*Monkey no. 1* (serial no. 12) showed 2.6 per cent infection of r.b.c.; given 20 mg. daily for 3 days— infection controlled. Relapse after 13 days; death 2 weeks later, 12 per cent infection of heart blood.

*Monkey no. 2* (serial no. 24) showed 15.2 per cent infection of r.b.c.; given 25 mg. daily for 3 days— infection controlled. Death after 9 days; heart blood negative for parasites.

*Monkey no. 3* (serial no. 31) showed 13.6 per cent infection of r.b.c.; given 25 mg. daily for 2 days— died after 3 days with 12 per cent infection of heart blood.

*Monkey no. 4* (serial no. 25) showed 2.6 per cent infection of r.b.c.; given 10 mg. daily for 4 days— infection controlled. Relapse after 13 days, infection rising to 16.4 per cent; given 25 mg.—infection controlled and animal alive after 177 days with chronic infection.

*Monkey no. 5* (serial no. 27) showed 2.4 per cent infection of r.b.c.; given 10 mg. daily for 5 days— infection controlled. Relapse after 17 days; treated with a different drug—animal died showing heavy infection with parasites.

*Monkey no. 6* (serial no. 33) showed 15.0 per cent infection of r.b.c.; given 10 mg. daily for 5 days— infection controlled. No relapse observed after 116 days—animal alive.

*Monkey no. 7* (serial no. 36) showed 13.2 per cent infection of r.b.c.; given 10 mg. daily for 5 days— infection controlled. Relapse after 14 days with chronic infection; no further treatment, animal alive after 110 days.

*Monkey no. 8* (serial no. 37) showed 7.8 per cent infection of r.b.c.; given 5 mg. daily for 3 days— infection controlled. Relapse after 16 days with chronic infection; no further treatment, animal alive after 92 days.

The experiments show that the butyl-acridine derivative has a powerful parasitocidal action on *P. knowlesi*. There was evidence of degeneration in the parasites the day after the first injection. The parasite counts decreased rapidly, and after the third injection, the blood was generally found to be free of parasites. However, in four out of the five monkeys which have survived after treatment, a relapse occurred, though only two appeared to require further treatment. The relapse infection in monkey no. 5 was used for purposes separate from the present investigation. The smaller doses of 5 and 10 mg. appear to be as effective as the larger doses, and were tolerated better. The monkeys treated with the larger doses have died, while four out of five treated with the smaller doses are still alive after relatively long periods. The reader is reminded that *P. knowlesi* is highly pathogenic to rhesus monkeys.

## Conclusion

Preliminary experiments with the butyl-acridine derivative show that the drug possesses

(Continued from previous page)

## Summary and comments

So far as we are aware, organic arsenicals have not been tried before in the treatment of simian malaria (*P. knowlesi*). Neither novarsenobillon ('N.A.B.') nor mapharside gave satisfactory results in the present trials, for in not one out of 14 monkeys treated with either of these drugs were parasites eradicated from the peripheral blood without the aid of other more efficient drugs. Both 'N.A.B.' and mapharside sometimes produced a temporary reduction in the infection rate of the red cells, and only in the cases of animals receiving 0.075 gm. or more of 'N.A.B.' did the infection rate show a continuous decline. Except with very large doses of 'N.A.B.' a parasitocidal action of the drugs was not much in evidence.

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(1939).

## RAPID STAINING OF MALARIAL PARASITES BY A WATER SOLUBLE STAIN

By JASWANT SINGH, M.B., Ch.B., D.P.H., D.T.M. & H.  
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and

L. M. BHATTACHARJI, M.B. (Cal.)  
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In recent years it has become increasingly difficult to purchase ingredients for the preparation of various modifications of Romanowsky stains, such as Giemsa, Leishman and Wright's, at a reasonable cost; if indeed they can be obtained at all. During the past year, work has been in progress in the laboratories of the Malaria Institute of India with the object of producing a stain in which readily available ingredients can be substituted for the costlier imported dyes and their solvents, such as methyl alcohol (acetone-free) and glycerine. Field (1941) described a method for rapid staining of malaria parasites in thick smears by which the common solvents were eliminated but which still involved the use of azure I\*. Simeons (1942) described another method of staining, using formulæ recommended by Stevenel (1918) and Boyé (1940) which did not involve the use of azure. This method is rapid and the ingredients used are inexpensive and easily obtainable; but the stain (J. S. B. stain) described below has certain additional advantages.

The history of staining with particular reference to the staining of blood and parasitic protozoa has been dealt with in detail by Conn (1930). Ehrlich (1879) had employed compounds of acid and basic dyes for staining blood cells, but Romanowsky (1891) was the first to demonstrate malaria parasites in detail by the use of a methylene-blue eosin combination. He remarked that old methylene-blue solutions on which a scum had formed gave better results than fresh ones. He also realized that some additional element was formed which gave a characteristic cherry-red colour to the

\* Field's article also described a satisfactory method of preparing a good stain from ordinary methylene blue.—EDITOR, I. M. G.

(Continued from previous page)

a powerful action against *P. knowlesi*. In view of its efficacy in small doses, comparative experiments with the amyl-acridine derivative are contemplated.

The authors are grateful to Messrs. Bengal Immunity for the generous supply of the butyl-acridine derivative.

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chromatin of the parasites. This additional dye was 'das rots aus methylen blau', subsequently known as azures I and II or methylene azure. This was first recognized as one of the components of polychrome methylene blue by Bernthsen (1885) and has subsequently been regarded as a mixture of azures and methylene violet, formed by the oxidation of methylene blue (MacNeal, 1925). This oxidation is known to take place in methylene-blue solutions upon standing and can be hastened by boiling the solution with alkalies (Unna, 1891); such an oxidized solution has been termed polychrome methylene blue. Leishman (1901) combined eosin with polychrome methylene blue and after filtering the precipitate, redissolved it in methyl alcohol and added water only at the time of applying the stain to the blood smear. But in view of the indefinite mixture of oxidation products, prominent among them being methylene violet (Bernthsen) and azures, different firms have put on the market components such as azure I, azure II, azure II eosin, etc., for the preparation of commonly used modifications of Romanowsky's stain. On account of the difficulties referred to above, we were obliged to start with methylene blue and the principle followed by MacNeal (1906), in preparing methylene azure has been revived with certain modifications. MacNeal prepared methylene azure by oxidizing methylene blue with potassium dichromate, in the presence of dilute hydrochloric acid. He found that methylene azure or azures A and B of Kehrman (1906), thus prepared, possess excellent staining properties for hæmatozoa.

Holmes and French (1926) found that the products obtained by acid oxidation of methylene blue, as described by MacNeal, are mainly the different azures A, B and C. These are not only more stable and homogeneous, but possess greater staining properties than those obtained by alkaline oxidation. According to these authors, polychroming in an alkaline medium gives rise to a decidedly heterogeneous mixture, containing hydrolysed products and azures, which being susceptible to further oxidation are likely to lose some of their staining properties. They therefore rejected the idea of employing alkalies and made use of acids.

### Method of preparation of water soluble stain

The stain consists of two solutions; I and II. The first is a solution of methylene azure prepared under acid oxidation and subsequently dissolved in a weak solution of a strong base, e.g. caustic potash.

#### Solution I.—

Medicinal methylene blue	0.1 gm.
Potassium dichromate ( $K_2Cr_2O_7$ )	0.1 gm.
Sulphuric acid ( $H_2SO_4$ ), 1.0% by volume.	0.6 c.cm.
Potassium hydroxide (KOH), 1.0%	2.0 c.cm.
Water	100.0 c.cm.

Dissolve the methylene blue in 100 c.cm. water by constantly shaking in a narrow-mouth flask. Acidify with the dilute sulphuric acid

and then add the chrome salt. A heavy deposit of flocculated amorphous purple-coloured precipitate forms. Shake thoroughly and heat the solution in a water-bath at boiling point. The original liquid and the precipitate begin to change colour, first becoming greenish and on further heating for about 3 hours at the above temperature the colour changes to blue. This change may be apparent after 2 hours of boiling but it is advisable to continue boiling for another hour. At the end of this period the flask is allowed to cool, and the precipitate\* appears as steel-blue needle-like branched crystals. Add 2 c.cm. of one per cent caustic potash solution drop by drop, while shaking the flask continuously, when the greater portion of the precipitate dissolves. This liquid is then filtered several times to ensure complete solution of the dye remaining on the filter paper. The filtrate is blue with a violet iridescence and is a mixture of the azures with only a trace of methylene blue.

The presence of methylene azure and traces of unoxidized methylene blue can be demonstrated by adding 2 drops of the filtrate to 2 c.cm. of water and 5 c.cm. of ether. On shaking vigorously for a few seconds, the ether absorbs the azures and turns faint orange or eosin red, while the watery layer below shows a faint blue colour due to the presence of some unaltered methylene blue. If instead of ether chloroform is added, this will settle at the bottom of the test tube, giving an intense violet colour which indicates the presence of azure. The watery portion at the top remains colourless. If the oxidation of methylene blue is incomplete the watery portion will stain a definitely blue colour. In actual practice a trace of unaltered methylene blue does not interfere with the staining.

*Solution II.*—This is readily prepared by dissolving one gramme of water soluble eosin in 500 c.cm. of tap water. A freshly-prepared eosin solution may not yield as satisfactory a stain as one which has turned deep red after some use.

Solutions I and II should be kept in wide mouth stoppered jars, 1½ inches diameter by 3½ inches height, and set aside for 48 hours to mature. These keep well for several months, but in solution I a thin golden yellow scum is likely to form on its surface due to slight precipitation of the dye. This does not, however, interfere with staining and the staining power of the solutions does not deteriorate with age.

#### *Method of staining*

The usual precautions in the preparation of blood smears are necessary. The slide should be as free from grease as possible. The thick

\* With concentrated sulphuric acid the precipitate gives a deep green colour thus indicating that it belongs to the thionin series like methylene blue (Holmes and French, *loc. cit.*). With ether it gives an orange-red colour showing that it is an azure (MacNeal, *loc. cit.*).

smear should be spread evenly, otherwise dehaemoglobinization and staining will not yield the desired results. The thin smear should preferably be one cell thick, so that the red blood corpuscles take up the stain uniformly. We have stained some old smears taken in the hot weather some months ago and have had consistently good results.

Thick and thin smears taken on the same slide can be easily stained.

1. Fix the thin smear by dipping that part of the slide in a jar containing methyl alcohol for a second or two.

2. Dry thoroughly, preferably by waving the slide in the air.

3. Immerse the whole slide in solution I for 30 seconds.

4. Wash in a jar containing acidulated tap water (pH 6.2 to 6.6). With tap water in Delhi (pH 7.6, indicator, bromo-thymol-blue) approximately 50 mg. of sodium dihydrogen phosphate or 5 drops of 5 per cent acetic or citric acid solutions for each 100 c.cm. of water are necessary.

5. Stain with solution II for one second.

6. Wash in the same jar (4) for 4 seconds.

7. Immerse in solution I again for 30 seconds (3).

8. Wash as above for 10 seconds or till the smear gives a pink background (4).

9. Dry and examine.

#### *Thick smear alone*

1. Immerse the slide in solution I for 10 seconds.

2. Wash in a jar containing water acidulated (pH 6.2 to 6.6) for 2 seconds.

3. Stain with solution II for 1 second.

4. Wash in the same jar (2) for 5 seconds.

5. Immerse in solution I again for 10 seconds.

6. Wash as above for 2 seconds or till the smear gives pink background (2).

7. Dry and examine.

The total time taken for staining a combined thick and thin smear is 1 minute and 20 seconds, and for a thick smear only 30 seconds. The latter period can be shortened to 10 seconds but with old or very thick smears it is preferable to follow the above timings.

When a large number of blood smears have to be stained, special racks holding 20, 25, 50 or 100 slides, and troughs of suitable sizes can be used to save time.

The results achieved with this stain have been striking, and the staining characteristics of the chromatin, cytoplasm, pigment and stippling can be differentiated in the same manner as with any of the Romanowsky stains.

In a thick smear, the malaria parasites show the usual appearances of the parasites with a background made up of haemolysed red blood corpuscles. The parasites may appear either free or within the red cells. The young parasites usually appear as rings, semicolon or semi-

lunar in shape, but they may be shrunken or distorted. The mature forms (trophozoites, schizonts and gametocytes) retain their shape well and the chromatin and cytoplasm stain intensely, with pigment showing up distinctly. Red blood cells infected with *P. vivax* show characteristic stippling. The Maurer's dots in *P. falciparum* infections can often be clearly seen.

In a thin smear, red blood corpuscles should appear faint pink or orange coloured, depending upon the extent of washing. The immature red corpuscles can be recognized by the polychromasia appearance of the cytoplasm and their characteristic nuclei. The other cellular elements of the blood stain in the same manner as with Giemsa or Leishman. Stippling in *P. vivax* and *P. falciparum* is seen better in a thin smear than in a thick. Stippling in *P. malariae* with this stain has not been observed.

This stain has been prepared on a number of occasions and has given consistently satisfactory results. It can easily be prepared in small laboratories at a very low cost. The chief points in its favour are :—

1. Costly ingredients, such as imported azures, glycerine and methyl alcohol which are not readily available, have been excluded and a watery base substituted.
2. Wastage in staining solutions has been minimized. The same solutions can be used for long periods with occasional replenishment.
3. The stain does not deteriorate with age and use.
4. The technique of staining is simple.
5. There is no necessity for using distilled water at any stage. Ordinary tap water or boiled water slightly acidified is all that is required.
6. Thick and thin smears taken on the same slide can be stained simultaneously in a short time (within one minute and 20 seconds) and a thick smear alone about 30 seconds. These timings can be varied slightly to suit individual requirements. The time taken in drying the film has not been taken into consideration as this will differ under varying atmospheric conditions.
7. Smears several weeks old can be stained satisfactorily.
8. The blood picture obtained in both thick and thin smears compares favourably with the original Romanowsky stain and its various modifications.

#### Summary

1. A new method of staining malaria parasites with a water soluble stain (J. S. B. stain) is described.
2. This method has the advantage of extreme rapidity, and the ingredients used are readily obtainable at a very small cost.
3. The stain can be easily prepared in a laboratory.

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## THE EFFECT OF QUININE AND STILB-AMIDINE (M&B 744) ON THE RETICULO-ENDOTHELIAL SYSTEM AS MEASURED BY THE CONGO-RED INDEX

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and

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THE mechanism of resistance, spontaneous or acquired, has not yet been elucidated in a clear manner compelling universal acceptance, but all workers in the field agree that the reticulo-endothelial system plays a very important rôle. Much work has been done on the part played by the reticulo-endothelial system in malaria, and of late years the phenomenon of phagocytosis in controlling malarial infection has received considerable attention.

In bird malaria, Cannon and Taliaferro (1931) observed that malarial parasites were phagocytosed at all stages of their development in acute primary infection. They also noticed a distinct activation of the mesenchyme which reached its maximum at the time of crisis during which the parasites disappeared rapidly from the blood. Sinton and Mulligan (1932) injected autolysed parasites into monkeys, producing intradermal reactions. Though there is no direct correlation between the occurrence of this reaction and the presence of demonstrable antibodies, Sinton and Mulligan (*loc. cit.*) are of the opinion that such delayed intradermal reactions result from a reaction between the antigen and an intracellular antibody in the reticulo-endothelial system. According to them

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4. The staining of the blood film compares favourably with that produced by any other method.

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the specific antibody is not humoral but cellular.

In human malaria, the phenomenon of phagocytosis was observed by Golgi as early as 1888, especially in benign tertian and quartan infections. Marchiafava and Bignami in 1894 noted that in malignant tertian malaria the leucocytes were engulfing not only cell debris but also the parasite and even the parasitized red cells, and thus removing them from the blood. Napier, Krishnan and Lal (1932) have confirmed these observations by the help of a supravital staining method. The work of Krishnan, Lal and Napier (1933) with a supravital staining technique has produced evidence to show that, in the process of phagocytosis in malaria, the monocytes and histiocytes are the principal cells involved. This phenomenon as it occurs in malaria has been found by Krishnan to be associated with a stimulation of the reticulo-endothelial system, as this reacts by the greater mobilization, proliferation, and an increased functional activity shown by the approach of these macrophages towards parasites and infected red cells and the final ingestion of the latter by the former.

The existence of a latent infection in a large percentage of cases of immunity to reinfection by malaria in monkeys (Krishnan, Smith and Lal, 1933 and 1934) may be understood in the light of this phenomenon. After the recovery from the acute phase or the primary attack, the process of phagocytosis goes on, and the immunological principle may be produced during the intracellular digestion of the parasites. When the infection is totally cured, there is evidently no further production of antibody, and the host loses its immunity. Taliaferro and Cannon (1936) suggest that antibodies are produced locally in sufficient quantities to be operative in the specific organs *in situ*, but not in sufficient quantities to be easily demonstrated in the peripheral blood.

Taliaferro and Mulligan (1937), in an extensive review of the literature, observe that in natural and acquired immunity the mechanisms are different. Natural immunity is non-specific and is not associated with an antibody, whereas the greatly superior mechanism for disposing of parasites which is associated with acquired immunity is highly specific and is probably associated with an antibody.

In a discussion of immunity in malaria Thomson (1933) stated that active phagocytosis by reticulo-endothelial cells of the spleen and liver was found in birds recovering from malaria. Yorke (1933) was of opinion that the reticulo-endothelial system did not play any essential part in the development of immunity (tolerance according to Yorke) in malaria, its function being merely that of a scavenger to clear up the debris. Brown and Broom (1935), and Chopra, Mukherjee and Krishnan (1935) have emphasized the importance of biochemical alterations in the blood and the parasites which facilitate the engulfing of the parasites.

It will be seen from the above that the reticulo-endothelial system plays a definite rôle in the cure of, and in the development of, immunity in malaria. It was therefore thought desirable to evaluate the efficiency of the reticulo-endothelial system in living animals by the congo-red method. It is however necessary to point out that objections have been raised against the usefulness of the congo-red test for an evaluation of the reticulo-endothelial function. Animal experiments have shown more or less definitely that the congo-red index has a direct connection with the phagocytic activity of the reticulo-endothelial system, but it must be admitted that this is only one of the many functions of the system. It would be certainly desirable to evaluate such functions as antibody formation, metabolism, etc., by suitable methods, but as long as such functional tests are not developed, it is justifiable to use the available method of congo-red index test.

The method is based on the fact that after intravenous injection, congo red, a colloidal dye, is stored by the reticulo-endothelial cells. Blood samples are withdrawn shortly after the intravenous injection of the dye, and later after a fixed interval of time; the concentration of the dye in the blood is found decreased in the second sample, thus permitting an estimate of the proportion of the dye which has been intercepted by the reticulo-endothelial system. The ratio between the dye concentrations in the two samples depends on the storing activity of the reticulo-endothelial system, and is termed the congo-red index.

*Method.*—A blood sample is first obtained from a monkey, and then 2 c.cm. of congo-red dye (1 per cent solution) is injected intravenously. Four and sixty minutes after the injection, blood samples are withdrawn, and the congo-red concentration in the plasma is colorimetrically determined. Just before performing the colorimetry, the congo red is transformed into the blue compound by the addition of hydrochloric acid and an acid buffer solution containing urea.

The congo-red solutions were sterilized before use. Merck's colloidal congo red was used for our experiments. The monkeys were always bled after fasting.

All three samples are centrifuged at high speed. After careful separation from the red blood corpuscles, 2 c.cm. of each sample are put into dry test tubes. To the colourless sample 1, obtained before injection of the dye, 1 c.cm. of 1 per cent of congo-red solution is added, and this serves as a standard. To this sample, as well as to samples 2 and 3 obtained four and sixty minutes after the injection of the dye, is now added 2 c.cm. of the buffer urea solution and 0.5 c.cm. of 10 per cent hydrochloric acid. A blue-violet colour develops, and colorimetry is quickly performed.

The details of the estimation of the congo-red index need not be given here. They are detailed



in a paper by Stern (1941). The congo-red index figure represents the proportion (per cent) of the congo red which has not been absorbed.

A higher numerical value of the congo-red index indicates that a smaller amount of congo-red has been stored by the reticulo-endothelial system, and therefore signifies that a diminution in its activity has taken place.

In all, 6 monkeys (*Macacus rhesus*) were used as experimental animals in 3 sets. The first set, consisting of 2 animals, was given quinine hydrochloride intramuscularly, the first receiving 1 grain daily, 11 injections in 14 days. The congo-red index was estimated after every 4th injection, the blood samples being taken one hour and a half after the quinine injection. This monkey, however, died as a direct effect of the toxic action of quinine after the 11th injection. The dose of quinine was reduced to  $\frac{1}{2}$  gr. daily in the second monkey which received 18 injections altogether in 30 days. The congo-red index was estimated after every 6th injection on an average. The blood samples were collected as before, one hour and a half after the quinine injection.

The second set consisted of one monkey only. It was given 10 daily intravenous injections of stilbene (M&B 744), 8 mg., the congo-red index being estimated after every 3rd injection. The blood samples were collected on each of these days one hour and a half after the stilbene injection.

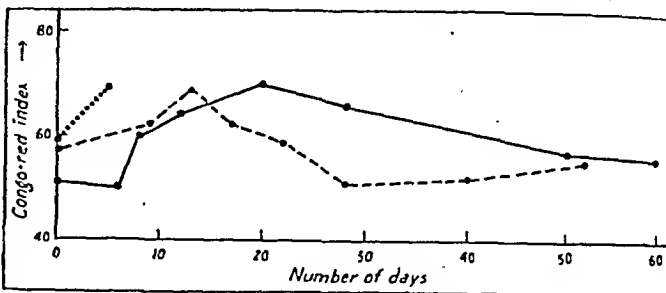
The third set consisted of 3 monkeys. They were infected with *Plasmodium knowlesi* obtained from infected monkeys. The intensity of infection was examined periodically and whenever the blood film showed heavy infection, a single injection of quinine hydrochloride in the dose 1 gr. or 2 gr. was given intramuscularly to control the intensity of infection, the first controlling injection of quinine being given after an initial period of 8 to 9 days of unchecked infection. (Occasionally the same dose or an increased dose had to be repeated next day as the initial dose did not reduce the intensity of infection.) The congo-red index was estimated in these infected monkeys at intervals, the first estimation being done when the infection was believed to be moderate as judged by the condition of the animal. The subsequent estimations were done at adequate intervals so that the bleeding (about 12 c.cm.) necessary for the test may not by itself impair the condition of the animal. The intensity of infection was judged by the condition of the animal and also by frequent blood film examinations. The congo-red index estimations could not be continued until the recovery of the animals.

The results are presented graphically.

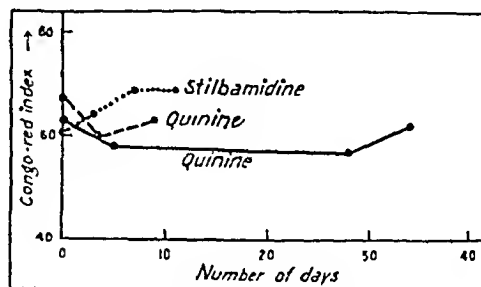
**Results.**—Quinine lowers the congo-red index only to a limited extent (about 6.5 per cent). Repeated injections of quinine in the doses given seem to depress the reticulo-endothelial system, and the congo-red index tends to rise after the

initial fall. Stilbene increases the index (12.8 per cent).

Effect of malaria infection on congo-red index.



Effect of quinine and stilbamidine on congo-red index.



**Malaria.**—In unchecked malaria the congo-red index increases (19.1 per cent), the rate of increase seems to be directly correlated with the intensity of infection. When the infection is controlled with quinine used in doses which proved to be rather toxic in normal monkeys, the congo-red index gradually fell to the pre-infection level, a fall of about 19 per cent, with the improvement of the general condition of the animal; the peripheral blood also showing diminution of infection.

**Discussion.**—From these preliminary experiments, the following generalization regarding the trend of immunity processes in malaria can be tentatively made. The increased intensity of infection corresponded with the fall of reticulo-endothelial efficiency as measured by the congo-red index; with the gradual increase of reticulo-endothelial efficiency, the intensity of infection diminished. Quinine was necessary to control the intensity of infection as also to reduce and gradually cure the infection. Quinine, by itself, slightly increases the reticulo-endothelial efficiency, but the increased efficiency of this system that is found in declining malarial infection is far greater. This increased efficiency must be the result of malarial infection as affected by quinine treatment. It is quite certain that, in the cell substance of the reticulo-endothelial cells, the engulfed malarial parasites are gradually digested. Quinine helps the increased phagocytosis of the parasites. This may be due to improvement of the reticulo-endothelial efficiency as measured by the congo-red index, and to the biochemical alterations of the blood facilitating phagocytosis as already mentioned. The intracellular enzymes responsible for the lysis of the parasite may act more

vigorously in the presence of quinine. It is known that quinine in very small concentration accelerates the action of autolytic ferments of liver and spleen (Cushney, 1941). The lysed malarial proteins modified by quinine may also act as antigens which stimulate the reticulo-endothelial system greatly and play the predominant rôle in increasing the efficiency of the reticulo-endothelial cells.

The observed tolerance of quinine by the malaria-infected monkeys merits careful scrutiny in formulating any theory of action of quinine in curing malaria. It is not likely that the destruction and excretion of quinine by the host tissues are greatly accelerated by the malarial infection. The most reasonable probability seems to be that quinine is absorbed by the malarial parasite. As a result, the effective concentration of quinine for the host cells diminishes. Quinine thus appears to have a special affinity for malaria parasites apart from any general effect on the reticulo-endothelial system. Immunity to fresh infection by malaria during the continuation of a malarial infection does not confer immunity to infection by other protozoal diseases which are immunologically associated with the reticulo-endothelial system. This phenomenon can only be explained by a specific immunizing process in malaria, very probably intracellular.

The increased congo-red index with stilbene (M&B 744), an effective leishmanicidal agent against kala-azar, also proves that the immunological processes in the two diseases are not the same.

**Conclusion.**—1. Quinine, in therapeutic doses, increases the efficiency of the reticulo-endothelial system.

2. Unchecked malarial infection depresses the reticulo-endothelial system, the degree of depression varies directly with intensity of infection.

3. When malarial infection is controlled with quinine, reticulo-endothelial efficiency increases as the intensity of infection declines. The percentage of the rise of phagocytic efficiency in malaria treated with quinine is far more than (more than double) the rise of efficiency with quinine alone.

4. Monkeys infected with malaria tolerated quinine better than normal monkeys.

5. A tentative suggestion regarding the mechanism of immunization and the special part played by quinine in that process is made.

6. Stilbamidine (M&B 744) does not increase the reticulo-endothelial efficiency.

Our thanks are due to Dr. J. Lowe, Professor of Tropical Medicine, School of Tropical Medicine, and Dr. B. S. Kahali, Professor of Physiology and Pharmacology, Ludhiana Women's Medical College, for helpful suggestions and criticisms.

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## A SIMPLE THICK DROP METHOD OF STAINING BLOOD FOR MALARIA

By H. T. INCE

CAPTAIN, I.M.S.

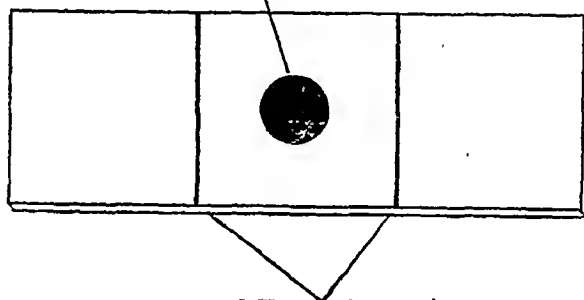
Combined Indian Military Hospital, Sangor, C. P.  
Requirements

1. Distilled water.
2. The usual Leishman stain—0.5 per cent in methyl alcohol. It should be made up in sufficient amount to last for a week. No other alcoholic solution should be substituted for methyl alcohol.

*Method of preparing and staining the film*

1. Take a fairly big drop of blood and spread to the size of a silver four-anna bit. Dry in

*Blood drop*



*Grease pencil marks*

air on the flat. (Don't cake the blood on the slide or it will wash off.)

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## PREPARATION OF A VITAMIN-A-ACTIVE MATERIAL FROM PLANT SOURCES

By K. C. SEN

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and

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VITAMIN A is considered to be one of the essential food factors required by all animals. Since it is not synthesized in either human or animal bodies, human beings and livestock have to depend on an external source of supply. With this vitamin partly or completely lacking, the chief symptoms seen in human beings are poor growth, night blindness, xerophthalmia, keratomalacia, phrynoderma, decreased resistance to all infective diseases in general and to respiratory disease in particular.

The main sources of the vitamin for human beings in their normal dietary are milk, butter, ghee, eggs, liver-meat, fish and green leafy vegetables. Vegetables do not contain vitamin A as such, but in the form of carotene which is converted into vitamin A in the animal body and is therefore known as the precursor of vitamin A, or as provitamin A.

Fish-liver oils, such as cod-liver oil, shark-liver oil and halibut-liver oil, contain vitamin A in large amounts. The livers of some domestic animals such as goats, sheep, cattle, etc., contain a fair amount of it; apart from these, the other animal products which are extensively used, namely, butter and ghee, contain some of the vitamin, but the amount is very variable, depending on the food of the animals. Cow's butter or ghee contains carotene in addition to vitamin A. While vitamin A is almost completely absorbed and utilized by the system, carotene is not so well absorbed, a good deal of it being passed in the faeces.

When vegetables are cooked, there is an unknown amount of destruction of provitamin

A, and owing to the variation in the amount consumed, it is difficult to estimate the vitamin-A intake of the average adult or child. The consumption of milk, butter and ghee is also very variable. In any case, these do not supply any very large amount of vitamin A to the adult, as the consumption of these products is usually small.

In view of the prevalence of avitaminosis A in this country, it has been found necessary to make use of some of the richer sources of vitamin A such as the fish-liver oils as a source of the substance. The Norwegian variety of cod-liver oil has had a big market in India, but owing to the war its supply has been stopped. Halibut-liver oil is another very good source of vitamin A, but it is not produced in India. Recently, considerable attention has been paid to shark-liver oil, and it is understood that a large quantity is now available from the Madras and Travancore Fisheries Department. When properly purified, it can be used as a good source of vitamin A.

For some years, workers in this country have paid some attention to alternative sources of this vitamin, and the observation on the vitamin-A potency of red palm oil aroused considerable interest. This material came mostly from Malaya and contains a number of pigments including the provitamin A. As far as is known, no attempt has been made to purify the material or to concentrate the active pigment, while attempts to get it used in vegetable ghee have not been very successful.

Although in various parts of the world a large number of vegetables have been examined for their vitamin-A potency, it is now established that no vegetable or plant sources are likely to be found to compare with some of the concentrated fish-liver oils in this respect. Consequently, where suitable fish-liver oils are available in quantity and where there is no prejudice against the consumption of these oils, there is little to be gained by an attempt to manufacture a vitamin-A-rich material from plant sources.

In India the problem takes a different shape. A large number of people who are vegetarians would prefer a product of vegetable origin. Fish-liver oils often have an unpleasant taste and smell, and may not be well tolerated by everybody, while in any case they sell at a high price in the Indian market; hence, a vegetable product rich in vitamin A, cheaply prepared and having no unpleasant taste, would have obvious advantages and commercial possibilities. If a suitable product can be manufactured, there is no doubt that it will be welcome by the public health authorities in India.

In view of these considerations, it is proposed to describe a method for manufacturing a vitamin-A-rich material from plant sources. This method was developed in connection with a programme of research connected with the determination of the carotene or vitamin-A potency

*(Continued from previous page)*

2. Grease pencil the slide on either side of the drop as seen in the figure.

3. When the slide is thoroughly dry, put 5 or 6 drops of distilled water on the drop of dried blood, and let stand for 2 minutes (this haemolyses the blood sufficiently). Then add the same amount of the Leishman stain to the distilled water and allow it to stand for 6 or 7 minutes. The slide is then rinsed in a basin of water. This should be done by taking the slide between finger and thumb, by the edges, and moving it a few times in the water *side ways*, and not with the flat surface of the slide against the water (this will wash off the film). Tap water can be used for washing.

4. The slide is then dried in air and examined like any other thick film.

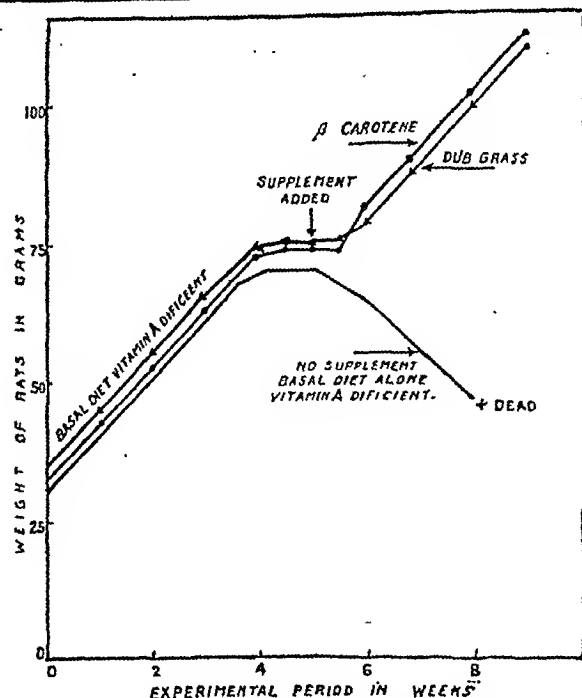
of various indigenous and cultivated pasture grasses and fodders of this country. In the course of this work over the last four years, the carotene content of various food materials has been examined, and many green grasses, legumes and cereal plants such as green barley, oats or wheat have been found to contain a very large amount of  $\beta$  carotene as determined by chemical, chromatographic and biological assay. This led us to study the possibility of utilizing this carotene both in the normal dietary and for therapeutic purposes by (1) drying the green plants and using them as such, (2) extracting the vitamin-A-active pigment in a comparatively pure form by means of a suitable solvent, and incorporating it in hydrogenated vegetable oils. These oils are now being extensively consumed by the general public, and are often used for adulterating ghee, which is itself a source of vitamin A.

The methods used are briefly as follows :—

### 1. Preparation of dry grass powder

Under this head, young cereal plants such as barley or oats, legumes such as berseem and lucerne, and grasses such as *dub* have been dried in a current of air at 60°C. The best results with cereals are obtained if the plants are grown in well-irrigated and well-manured land with plenty of sunshine. The plant samples should be taken at 24 to 40 days' growth, when there should be a moisture content of, roughly, 85 to 88 per cent. The freshly-cut material should be placed in a tunnel drier, without being unduly exposed to the sun and without mining, and dried as rapidly as possible. It is easy to obtain within a few hours a product having 96 per cent dry matter. The material can then be powdered and stored. The vitamin-A potency of the original plant remains unaltered when the plant is dried at a low temperature and it can be preserved in a refrigerator for over two years without much loss. Different lots of the dry material obtained at different times from barley plant or *dub* grass have given carotene values ranging from 350 to 600 micrograms per gramme of dry matter. Biological assay has shown this grass carotene to be absorbable to the same extent as pure  $\beta$  carotene obtained from the market (*vide* figure). Assuming an average value of 400 micrograms per gramme of the dry powder, a daily consumption of 5 grammes of the powder would meet the requirement of an adult.

The dry barley or *dub* grass powder has not an unpleasant taste and can be made more palatable, if necessary, by mixing with a little sugar, syrup, or honey before it is eaten. An additional advantage of using this grass powder is that, apart from carotene, young grass contains other vitamins as well. A recent American report states that grass contains a high amount of vitamin K<sub>1</sub>, tocopherol, ascorbic acid, riboflavin, pyridoxine, biotin, thiamin, niacin, pantothenic acid and choline, in addition to carotene.



In short, grass powder is a multiple vitamin product. So far as vitamin-A potency is concerned, the following table shows the relative carotene and vitamin-A content of fodder plants, edible vegetables and other food materials :—

TABLE

Source	Carotene or vitamin A in micrograms per gramme dry material
Cabbage ..	200-300
Spinach ..	250-350
Carrot ..	100-200
Lettuce ..	300-350
Berseem ..	250-400
Lucerne ..	250-400
Barley plant ..	400-600
Oat plant ..	350-550
Wheat plant ..	350-550
<i>Dub</i> grass ..	300-400
Elephant grass ..	200-300
Red palm oil ..	400
Cod-liver oil ..	650
Shark-liver oil ..	2,000-7,000
Halibut-liver oil ..	6,000-12,000
Cow's butter ..	3.5 (carotene) + 12.0 (vitamin A).
Egg (fowl) ..	10.0 (carotene) + 5.0 (vitamin A).

Note.—Weight for weight, vitamin A is approximately twice as active biologically as  $\beta$  carotene.

It will be seen that fodder plants are a much richer source of carotene than some of the vegetables used in the human dietary, although specially grown vegetables may give higher values.

The dry grass powder as described above cannot, however, be mixed with vegetable fats, and in order to obtain a product which can be utilized for fortifying vegetable ghee or

(Concluded on next page)

# MAHWA YEAST FROM AN ALCOHOL FACTORY AND ITS VITAMIN CONTENT

By M. B. DAVER

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and

S. SHAFIUDDIN AHMED

The importance of yeast as a rich source of B vitamins has been recognized from the very beginning of vitamin research. Funk in 1911 first pointed out that yeast was a rich source of the beri-beri curative substance. Goldberger

(Continued from previous page)

margarine, it is necessary to extract the carotene pigments.

## 2. Extraction of carotene

Extraction of carotene from the dried materials described above is easily effected with petroleum ether. The extract contains not only the carotene but also other yellow pigments, as well as green chlorophyll. However, by passing the extract through a column of specially prepared calcium phosphate, it is possible to obtain only the vitamin-A-active carotene pigments, with a small percentage of fat present in the original grass. The extract, after being passed through the adsorbent column, is evaporated and an orange-red solid residue is left which in the presence of a stabilizer such as hydroquinone, and under an inert gas, can be preserved for a long period without any deterioration of the vitamin-A potency. This material can be easily incorporated in any vegetable fat to give the same level of vitamin-A potency as is found in natural butter, and without giving any undue colour or taste.

Large-scale production of carotene from these plant products is now being undertaken in collaboration with Professor G. Sankaran of the All-India Institute of Hygiene and Public Health, Calcutta. Quite recently we have found that tender leaves of water-hyacinth, which is a pest in Bengal, is as rich in carotene as some of our pasture grasses, and it appears to us that we can utilize this material instead of the more valuable cereal plants or pasture grasses for the large-scale production of carotene. We believe that the extraction of carotene from water-hyacinth will be found economical, and that, at the present moment when there is a large demand for carotene for both civilian and army consumption, the utilization of water-hyacinth as the raw material will not only give us a valuable food factor, but will also help to remove a pest from Bengal. It is also desirable to make an assay of some of the aquatic plants commonly found in the coastal areas, as it is likely that some of them might be found to be rich sources of carotene.

We are grateful to Dr. F. C. Minett, Director of this Institute, for his interest and constant encouragement.

and Tanner (1925) introduced yeast in the treatment of pellagra. Goodall (1932) advocated its use in certain types of macrocytic anaemia. Various workers have shown that angular stomatitis and glossitis can be cured by yeast, an effect due to its content of riboflavin and other vitamins of the B<sub>2</sub> complex.

While it is a known fact that yeast is rich in B vitamins, its potency in the various vitamins differs according to the strain of yeast and nature of media used. Yeast grown on media which is rich in B vitamins contains an increased amount of the B<sub>1</sub> and B<sub>2</sub> vitamins.

Swaminathan (1942) has analysed samples of dried yeast and has shown that torula yeast grown in molasses solution compares favourably in its vitamin content with brewer's yeast. He found distillery-yeast samples to be poorer sources of these vitamins. Recently a few samples of 'mahwa' yeast, obtained from our State Alcohol Distillery at Kamareddy, were sent to the Coonoor Research Laboratories to see if they were rich in B vitamins. The results of the analysis showed that the samples differed much in their vitamin values, but compared favourably with torula yeast and were better than distillery yeast.

Before the vitamin values are compared, it will be of interest to describe briefly how 'mahwa' yeast is obtained, during the process of alcohol distillation.

'Saccharine matter is extracted from mahwa flowers by boiling them in water. The juice is sterilized, cooled and then inoculated with sterile yeast culture prepared from mahwa flowers. After the completion of the fermentation, juice is distilled and the sediment of yeast remains behind in the fermentation vats. To the fermentation vats, ammonium sulphate is added, as it acts as a nutrient for the yeast.'

From the table below it is seen that there was considerable variation in the amount of various B vitamins present in different samples of yeast, even though the samples of yeast were of the same kind and grown on a similar medium. These wide variations may be due to sampling errors and methods used in drying. It is known that the procedure adopted for drying certainly influences B<sub>1</sub> content. In the circumstances we might justifiably take an average of the series of tests as giving average figures for B vitamins.

For the sake of comparison, results of analyses by Swaminathan (*loc. cit.*) are also shown in the table.

In the table, the riboflavin values for mahwa yeast are not given. These are probably of the same order as those of other kinds of yeast.

From the above it will be seen that the vitamin B<sub>1</sub> and nicotinic acid content of mahwa yeast was decidedly more than that of the distillery dried yeast. The values compared favourably with those of brewer's or torula yeast. Mahwa distillery yeast could be used effectively for medical purposes. It may be added that it is more palatable than either brewer's or torula

TABLE

The vitamin B<sub>1</sub> and nicotinic acid content of mahwa yeast as compared with values reported for torula yeast and distillery yeast.

RESULTS OF ANALYSIS PUBLISHED BY SWAMINATHAN						RESULTS OF ANALYSIS OF DRIED MAHWA YEAST OF ALCOHOL FACTORY	
Sample number	Variety		Vitamin B <sub>1</sub> , μg./g.	Riboflavin, μg./g.	Nicotinic acid, μg./g.	Vitamin B <sub>1</sub> , μg./g.	Nicotinic acid, μg./g.
1	Yeast, dried, brewer's	..	42.1	52.3	464	..	..
2	Do.	..	34.0	55.4	430	..	..
3	Do.	..	21.0	44.6	400	..	..
4	Do.	..	33.6	48.5	412	..	..
5	Yeast, dried torula, grown in synthetic medium containing molasses.	(1)	26.1	64.8	195	..	..
6	Do.	(1)	25.4	55.6	165	..	..
7	Do.	(1)	24.1	71.5	180	..	..
8	Do.	(1)	22.8	84.7	261	..	..
9	Do.	(1)	33.3	62.0	200	..	..
10	Do.	(2)	33.3	68.0	190	..	..
11	Do.	(2)	41.2	55.0	200	..	..
12	Do.	(2)	28.0	74.0	337	..	..
13	Yeast, dried, distillery	..	12.9	32.5	90	54.2	400.0
14	Do.	..	10.4	23.2	65	30.0	165.0
15	Do.	..	11.2	22.4	63	9.6	366.9
16	Marmite	..	12.5	89.2	665	24.0	125.0

yeast, and since it is a waste product it could be sold at a cheaper rate.

#### Summary

1. The vitamin B<sub>1</sub> and nicotinic acid values of dried mahwa yeast, from an alcohol distillery, have been compared with those of brewer's yeast, torula yeast and distillery yeast.

2. Steam dried mahwa yeast gave high values equivalent to those given by torula yeast grown on a molasses-salts medium.

#### Acknowledgment

We are grateful to Lieut.-Colonel K. N. Waghrey, Director, Medical and Public Health Department, for his permission to publish this article and are greatly indebted to Dr. M. Farooq, Deputy Director of Public Health, for his help and guidance.

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#### ON HUMERO-SCAPULAR PERIARTHRITIS

By DOZENT DR. GEORG POLITZER

(From the Princess Surrendra Kumari Memorial  
Central X-Ray Institute, Patiala)

IN the year 1872, Duplay described a disease of the shoulder characterized by restriction of the movements in the shoulder-joint and by pains over the greater tuberosity of the humerus. The diagnosis of this disease was rather uncertain, as it was often mistaken for muscular rheumatism or incipient arthritis. The introduction of x-rays facilitated the differential diagnosis of this disease, as a marked shadow is often visible near the great tuberosity of the humerus (*vide* figure 1). The disease was first called Duplay's disease; later, because of its specific localization, 'humero-scapular periartthritis'. Later still attempts were made to find similar changes in or near other bursæ of the human body, and the name of 'bursitis calcarea' has been proposed.

As far as the anatomical localization of these shadows is concerned, the opinions of the



different authors disagree in all essential points. Codman (1906, 1908, 1911, 1912), one of the first who described the shadows, localizes them in the tendon of the supraspinatus muscle. Others—especially French and German authors—describe a greyish calcified 'smear' filling the subacromial (or subdeltoid) bursa. Recently the question has been decided by Wrede and especially Bartels (1940) who have operated on dozens of cases. They find the calcified masses sometimes in the bursa, sometimes under the synovial cover of the supraspinatus muscle. Some small deposits may even be found between the fibres of the tendon.

Another group of authors has drawn attention to the fact that occasionally calcifications are found without clinical symptoms, while sometimes calcifications are absent in spite of



Fig. 1.

the typical clinical features of the condition. Koehler (1935) goes so far as to deny that the calcifications have anything to do with Duplay's disease, but considers the coincidence of clinical and radiological symptoms as merely accidental. This opinion is surely wrong; in my experience, which is supported by observations of the recent authors, calcifications are present in about 90 per cent of the cases of Duplay's disease.

A most astonishing fact is that, although tendons and bursæ exist in abundance in the human body, attempts to find similar changes in other areas have not been successful. Some small calcified spots have been found occasionally in the prepatellar bursa in persons who habitually work in the kneeling posture (char-women). These small calcified spots were undoubtedly of

traumatological origin, and it was impossible to establish any convincing relation to the above disease, as they were different in their histological features, in their cause, and, as is pointed out later, in their response to x-ray treatment. The only joint for which the existence of a similar disease is still claimed is the hip-joint. Especially the case of Ehrlich (1928) has been mentioned in many textbooks (e.g., Schinz *et al.*, 1932). Calcified spots were visible over the area of the joint space. Contrary to this, a case in my own collection showed a bean-sized calcified body above the great trochanter. Goldenberg and Leventhal (1936) reported calcifications in some of the muscles round the hip joint. These cases are exceedingly rare, and none, as far as I know, has been examined histologically. Furthermore the localization of the calcified bodies varied so markedly that no true characteristic of the disease can be established. Hence the majority of authors have reverted to the previous names (Duplay's disease or humero-scapular periartthritis) as the attempt to label this condition as a local manifestation of a general disease of the bursæ has failed.

It is even more difficult to relate the shadows near the shoulder-joint with the not uncommon calcification of tendons. These ossifications affect especially the insertions of the tendons, and the shadow shows clearly the form of the tendon, while the calcifications in cases of Duplay's disease are without connection to the bone and are of no characteristic form.

Another observation has been made which indicates the specificity of the disease. Between 1925 and 1930, several articles appeared in French journals reporting that balneotherapy, diathermy and x-ray therapy have not only improved the clinical condition of the patients suffering from this disease, but that the calcified spots over the area of the bursa, clearly visible in the x-ray pictures taken before the treatment, have vanished completely. As it was only too well known that soft tissue calcifications, as in cases of ossificant myositis, ossificant tendinitis, Stieda's shadows, etc., are absolutely refractory to x-ray treatment, the accuracy of these reports of the French authors has been doubted, especially as the reproduction of the x-ray pictures attached to the papers was so bad (as is usual in French scientific papers) that they did not convince the reader. Nevertheless they encouraged me to repeat these experiments, and most of the calcifications in cases of Duplay's disease disappeared after x-ray treatment.

I report a case of my own observation: The left shoulder-joint showed a calcified spot of  $\frac{1}{2}$ -inch length and  $\frac{1}{4}$ -inch breadth lying over and slightly lateral to the tip of the greater tuberosity of the humerus. The structure of the calcification was homogenous and the outline rather sharp. Clinically, slight pains, heaviness of the arm and remarkable restriction in mobility were present. After 4 months of treatment (monthly two treatments of 200 R

each) all clinical symptoms were gone. X-ray pictures were made at regular intervals, and they showed the gradual diminution of the calcified spot in size and density. After four months, only very small remnants of the former calcification were traceable. The treatment was stopped, but the patient was re-examined after three months. It was interesting to see that in the picture made after these three months, no calcification at all was visible although no further treatment has been given during this period. Other observations of myself and of other authors [*vide* Mustakallio (1939) who treated 113 cases, out of which 71 were cured] tally well with above report. Thus it can be said that the calcifications in the cases of Duplay's disease are usually not permanent, like most other soft tissue calcifications, but disappear after treatment.

All this shows clearly that the disease of Duplay is a pathognomonic entity characterized by a specific localization, clinical features and reaction to x-rays. As there are many other bursæ (and tendons) in the human body, it is difficult to understand why only one should be subject to the occurrence of a special disease. The explanation might be in the presence of some special anatomical or physiological features by which the subacromial bursa differs from other bursæ. Studies of this matter were therefore undertaken. Most cases look similar to that represented in figure 1. It shows a homogeneous calcification above and slightly lateral to the greater tuberosity; there are, however, exceptions to this. I selected for study 20 of my own cases. Dozent Fritz Eisler contributed another 14. The radiograms of all the shoulder-joints were reduced to the same size, and all the calcifications found in the different cases were projected one over the other. The diagram, which cannot be represented here (as it has been lost during the occupation of Austria), showed the overwhelming majority of the calcifications at the place mentioned above. A few were localized medial to the typical position, and some were more distal to the greater tuberosity, the lowest slightly above the deltoid tuberosity. It was already known that occasionally the calcifications in cases of Duplay's disease are localized a little more distally, and some authors have presumed that this may be due to the fact that they affected the subdeltoid bursa (instead of the subacromial bursa); this idea is mentioned in the textbooks of anatomy also after the introduction of the Basle nomenclature. Others thought that in these cases the calcification affected the deltoid muscle instead of the tendon

of the supraspinatus muscle, although it seems that none of these cases has been examined anatomically. Nevertheless the x-ray picture (as explained below) did not produce evidence of the existence of such a bursa. If a subacromial as well as a subdeltoid bursa did exist, and if the calcifications of the Duplay's disease could affect either one or the other, the diagram mentioned above should show two points of greatest affection, one above the greater tuberosity and one over the deltoid tuberosity. In fact there is only one centre, over the greater tuberosity, while the calcifications are less frequent as we proceed downwards from this spot.

The next step was a careful study of the development of these lesions. I began with the dissection of the shoulder-joint of older embryos and of young children and found that there is no independent appearance of a subdeltoid bursa. The only formation visible in these earlier stages is the primordium of the subacromial bursa. When I proceeded to study the condition in adults, I was informed by Pfuhl (1933) that he had nearly completed a study about these bursæ in adults. Later (1933) a detailed study on this subject appeared in volume 73 of the *Morphologisches Jahrbuch*. The result of this study is best explained by the help of figure 2 of this paper which is drawn after figure 17 of the paper of Pfuhl (1933). It shows that there are no separate subacromial and subdeltoid bursæ, but a common space which extends medially beyond the acromion,

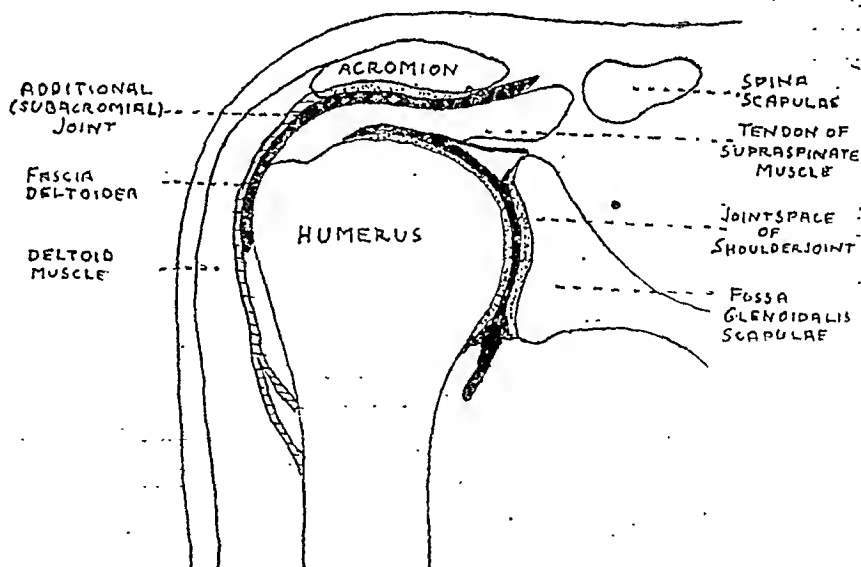


Fig. 2.

while its distal end lies sometimes below the greater tuberosity and in other cases well below. A single cavity is usually found but sometimes there are some small septa which subdivide it incompletely into several chambers. Nevertheless Pfuhl (1933) proves that, however these septa may be developed and however far this cavity may reach distally, the bursa is to be considered as a morphological and functional

unit. Studying carefully the conditions of the tissues surrounding this cavity and its function with the mechanism of the shoulder-joint, he rightly considers the whole formation as an additional joint to the shoulder-joint and calls it therefore 'subacromial additional articulation of the shoulder-joint'. The concavity of this joint is formed by the subacromial facet of the acromion, the coraco-acromial ligament and occasionally a part of the coracoid process and the origin of the coraco-brachial ligament. The convexity of the joint is formed by the tuberosity of the humerus and by a disc in the formation of which the tendons of the supraspinatus, infraspinatus, and subscapular muscles and the coraco-humeral ligament participate. This additional joint shares remarkably the movements of the shoulder-joint, although the exact data about the amplitude of these movements seem to have not yet been published. Pfuhl himself has already mentioned that this additional joint shows often changes typical of arthritis deformans.

These observations of Pfuhl (1933), together with my own findings, explain some of the specific features of Duplay's disease. Morphologically and functionally the so-called subacromial bursa is completely different from all other bursæ of the human body. Also the unusual arrangement of the disc and the supraspinatus muscle, being covered by the synovial membrane of the bursa, indicates relations between tendon and synovial membrane which are hardly comparable with the conditions in any other part of the human body. So it is not astonishing that this region should be subject to a disease not to be found in other parts of the body. The participation of the bursa in the disease cannot be denied. Either the wall formed by the disc and tendons is affected, when a reactive exudation into the bursa is unavoidable, or the bursa itself is filled with pathological calcified masses.

These special anatomical features of the 'additional joint' fit in well with the symptoms of Duplay's disease. The importance of the additional joint (bursa) for the movements of the shoulder explains the early occurrence of restriction of the movements of the shoulder-joint in cases of Duplay's disease. But it explains even another outstanding symptom of this disease which patients usually complain of, the heaviness of the arm. Now it is well known that the weight of the arm is not carried by the muscles alone, but first of all by the joints. The joints contain only very small quantities of synovial fluid under normal conditions, and the weight of the arm is borne by the negative pressure resulting from the airtight juxtaposition of the joint facets. The weight carried in this way can be easily calculated from the size of the opposing facets. For the average adult the facet of the shoulder-joint measures about one square inch, which corresponds to a support for a weight of 13 pounds. The average

(Concluded at foot of next column)

## SOME OBSERVATIONS ON ECTOPIA LENTIS

By S. N. MITTER, B.Sc., M.B., B.S., D.O.M.S. (Eng.)  
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A DEFECT in the zonule of Zinn may occur in the lower part of the circumference of the lens. Such a defect may be caused by—

(a) An imperfect or delayed closure of the foetal ocular cleft; this prevents the ciliary body

(Continued from previous column)

size of the facets of the additional joint measures half a square inch and the support therefore is 6½ pounds. If now the walls of the so-called subacromial bursa are not attached to each other as usual, but are separated by pathological masses or by exudates, this support is diminished or reduced to nil. This causes the subjective impression of heaviness of the arm.

**Conclusion.**—Duplay's disease is characterized by certain specific features. The calcifications present in the overwhelming majority of the cases lie usually above and lateral to the greater tuberosity of the humerus, but they are found occasionally medial and distal to this position. The calcified spots in cases of Duplay's disease disappear often after x-ray treatment, while other kinds of soft tissue calcifications remain unchanged. There is no other joint or bursa in the human body in which the existence of a disease similar to Duplay's disease has been proved. These specific features of Duplay's disease are explained by the special morphological and physiological characters of the so-called subacromial bursa as pointed out by Pfuhl (1933) and myself. These investigations have shown that the so-called subacromial bursa is really an additional joint which contributes remarkably to the amplitude of the movements in the shoulder-joint as a whole. The main clinical features (pains, restriction of movement, heaviness of the arm) can easily arise from the anatomical and physiological qualities of this additional joint.

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from coming into contact with the lens in this area during development, resulting in the non-formation of zonule of Zinn in that area.

(b) The presence of microphakia. This is really a condition in which the globe and the cornea pursue their usual growth, whereas the lens remains small. In this process, the zonular fibres are ultimately overstretched, and may tear away at certain points.

(c) The presence of buphthalmia and certain unusual causes of myopia. Here too the fibres are overstretched. These conditions, and therefore the resulting overstretching, occur after birth, and are, strictly speaking, non-congenital.

There are different degrees of the defective formation of the suspensory ligament of the lens. There may be a complete absence resulting in a mobile lens; there may be a partial or total absence of fibres in a particular area, usually the lower and inner part of the circumference; there may be an increased fibrous tissue formation in a particular area, resulting in an unequal traction on the lens as the ciliary body grows away during the course of development.

One of the results of such a defect in the zonule of Zinn during development is a congenital dislocation of the lens.

The following case record and family history should be of interest :—

#### *Case history*

P., Hindu male, aged 25, attended hospital in November 1935, with intense headache and marked redness in the right eye. Cornea hazy, anterior chamber deep, and containing in the bottom what appeared to be the lens nucleus. Tension 55 (Bailliant). There was a history of prolonged fever in October 1935, followed by dimness of vision in the right eye; this was followed by the present condition. There was no history of trauma. The condition was diagnosed as secondary glaucoma, and conservative treatment having failed, enucleation was advised, which the patient refused. He attended again in January 1936, when he had in the right eye a large ciliary staphyloma, with no perception of light. The lens nucleus was still in the anterior chamber, but the eye was quiet. During this time he was under treatment elsewhere, where the lens nucleus was considered to be an exudate, and he was given 14 injections of tuberculin on the supposition that he had tuberculous iridocyclitis in the right eye. On this occasion his left eye was examined. Vision 2/60, with his glasses, which were + 12 D sphere, 6/9. Anterior chamber was deep; the eye was aphakic; the capsule was seen flopping about behind a tremulous iris. No trace of the lens could be seen and there was no history nor any evidence of any operative interference. The fundus was normal.

He narrated the following interesting history. He always placed reading matter very close to his eyes in childhood. In 1923, when he was aged 12 years, he was shown to a specialist, mainly for dimness of vision; 2 subconjunctival injections of cyanide of mercury were given, but as there was no improvement, he refused further interference. He was prescribed - 8 D sph. in both eyes, which he used for a few years. In 1927 he consulted another specialist who advised operation and prescribed + 14 D sph. in either eye; he refused operation as he saw much better with these glasses. He then consulted another specialist who agreed with the number of the glasses and advised the patient that he had cataract: this specialist was, however, not willing to operate straightway. In 1928 the patient came back to the same specialist who had seen

him in 1923, and had then prescribed myopic lenses. He was, however, this time prescribed R.E. + 12 and L.E. + 15; with a + 2 D sph. more for reading in either eye. He is now wearing these glasses.

He was a tall, thinly-built person. Besides arachnodactyle, he had a cubitus varus of the right elbow-joint which could not be extended beyond 145 degrees. This defect has been present since infancy: his other joints showed complete freedom of movement.

It is interesting to watch the progress of ectopia lentis, and it fairly commonly ultimately ends as in the above case. The condition must have been very slight in 1923, probably the aphakic portion of the pupil causing much annoyance, and practically no improvement being seen with his myopic glasses. By 1927, the ectopia lentis had advanced to a marked extent, leaving a larger aphakic area of the pupil, so that hypermetropic glasses were now substituted; the lenses were probably present in the pupillary area, as opinions for and against their removal were given by two specialists. In 1928, however, the question of operation did not arise. By 1935, the right eye was destroyed by secondary glaucoma, while, fortunately for the patient, all that remained in the left eye was a shred of capsule. It was probable that he was really a case of microphakia, in whom the lens of the right eye moved freely into the anterior chamber and determined the secondary glaucoma, later.

While his history was being taken, he said that all his children were short-sighted. He had 3 sons and 1 daughter. He was asked to bring for examination his wife as well as his children. They were examined in December 1936 under a mydriatic. No abnormality could be detected in the wife; she was a healthy, fairly intelligent woman with a normal vision. She met with an accident on 3rd November, 1935, and her husband said that, due to the anxiety caused by her condition, he got his first attack of pain in his right eye on 5th November, 1935. The children were all healthy and intelligent: the most intelligent of them had the most defective vision. They all showed arachnodactyle, and, excepting the youngest child, they all showed in their right elbow-joint the same defect as their father. Their records are summarized as under :—

O. P., male, aged 9 years, R.V. 6/36; L.V. 6/36; lenses dislocated directly upwards; about 1/5th of the pupillary area is aphakic. Fibres of the zonule of Zinn seen from the lens margin, most of them are curled up, only a few being attached just behind the iris. With - 10 D sph. combined with a - 1 D cyl. axis vertical, vision improves to 6/12 in either eye. This can be compared to his father's condition in 1923.

N. P., male, aged 8 years, R.V. 1/60; L.V. 2/60. Lenses dislocated upwards and outwards very markedly in either eye. About 5/6ths of the pupillary area is aphakic. No evidence of zonule of Zinn in the middle of the lens margin, but fibres are present in the edges. With 12 D sph. vision is 6/60 in either eye. This child attended hospital again in February 1939 with a secondary glaucoma in the left eye. The lens had moved into the anterior chamber completely. The eye became comparatively quiet in a few days; an attempt was made by me to remove the lens, but it slipped back into the posterior chamber. The eye, however, remained quiet for a year and a half, though sight

gradually deteriorated, and could not be improved further with glasses. The child died in 1941 of enteric fever.

S., female, aged 6 years, R.V. 2/60; L.V. 2/60; lenses are dislocated upwards and inwards in both eyes fairly markedly. About 4/5ths of the pupillary area are aphakic. Some fibres of the zonule of Zinn are seen stretching completely. Vision could be improved only in the left eye with + 17 D sph. to 6/15.

S. P., male, aged 4½ years; lens margin could not be seen in the pupillary area. Iris was not tremulous. The anterior chamber in each eye was definitely deeper in the lower area. There was a hypermetropic astigmatism in either eye amounting to + 0.50 D cyl. axis vertical. It is extremely probable that in course of time this child will also show an ectopia lentis upwards.

It will thus be seen from the above history that a man with ectopia lentis married a normal woman, and all the four children born showed ectopia lentis in different degrees. They all showed arachnodaetyle, while all except one showed a defect in their right elbow-joint involving muscles and tendons, similar to their father. This is in confirmation of the hereditary factor observed in such cases that the dominant is the abnormal, and that in the offspring there is a complete preponderance of the abnormality. The patient had no sibling; his father had also suffered from 'weak eyesight' since childhood and till his death. It is quite likely that he too had a congenital anomaly of the lens, so that this defect seems to have been present in three generations.

There is, however, not always a preponderance of the abnormality in the offspring: the following is an example of a case in which, in spite of the case being very widespread and advanced in the patient, two other siblings had no defect whatsoever, and the parents and the grandparents showed no abnormality.

S. G., male, aged 13 years, came for a private consultation in October 1941. R.V. 6/60, with 11 D sph. 6/9; L.V. 6/60, with 12 D sph. 6/9; near vision J 1, with 3 D sph. more. There is almost complete luxation of the lens downwards, the right having moved much further down than the left. The undilated pupillary area is aphakic: no coloboma of the lens; zonular fibres cannot be seen. The iris pattern was not clear, and the pupils, though regular, did not dilate properly with atropine. The boy had a good memory, was intellectually very sharp, and was rather temperamental. He was tall, thinly built and showed a pigeon-breast and very typical and marked arachnodaetyle. Physician's examination revealed congenital pulmonary stenosis. He was born a premature child, and the mother had a tumour in the abdomen removed within a year of the birth of the child. When the child was aged 2 years the parents noticed that the child began bringing objects very close to the eyes to see. His general health was very poor; he had prolonged medical treatment in Calcutta, where various injections and ultra-violet exposures were given. No history of infantile convulsions. He was first given glasses in 1936, 12 D sph. There was no history of any redness or any other trouble in the eye. The boy died in 1942 following a sudden heart attack.

Ectopia lentis is a rare condition. Clapp (1934) mentions that it is noted once in 10,000 cases; our impression is that it is still rarer, one case having been noted in a hospital attendance of 25,000. Wright and Nayar (1936) say that microphakia, which is one of the conditions most

frequently giving rise to ectopia lentis, is seen once in 4,000 cases; statistics of the Madras Hospital show 5 cases in 21,000 in 1926, none in 1927, none in 1928, 1 case in 1929 in an attendance of 27,113, one in 1930 (28,470) and 7 in 1931 (28,831). It is quite likely that the higher figures are the result of calling in the family of the patient, which would certainly increase the incidence.

The condition is hereditary and bilateral. Roesse (1933) has given a record of four generations, while Lewis shows a record of six generations. As in the present instance, a large number of cases in the offspring are affected. Ridley and Sorsby (1940) have given instances and illustrations of a family described by Werc in which the father and his three children are affected. The condition is very frequently associated with arachnodaetyle while many other malformations in tissues arising out of the mesoderm occur: bones, ligaments, muscles, tendons and connective tissue, heart and blood vessels are affected. Extensive involvement of mesodermal tissue is illustrated by Maxwell (1937) who gives a detailed description of a case; the boy, an orphan, was also mentally subnormal. In the family now reported, besides arachnodaetyle, the right elbow-joint showed a cubitus varus in all cases. In the last case described above, extensive defects in the cardiovascular system were noted. Wright and Nayar mention a case in which a skeletal state converse to that of arachnodaetyle was noted with microphakia. In view of these extensive mesodermal defects present in association with ectopia lentis, Sorsby has expressed doubts whether the suspensory ligament is ectodermal in origin.

The ultimate fate of these eyes remains always a matter of concern. In view of the fact that the suspensory ligament is weak, stretched, and often absent in places, and in view of the fact that the size of the lens is frequently smaller than normal, the lens tends to move freely. A subluxation may become complete, and glaucoma may develop, as happened in the patient and one of his sons. The condition thus becomes difficult to remedy, and the eye is often lost with ciliary staphyloma, as in the present case. It may be noted that this happens almost solely where the lens moves into the anterior chamber. No trouble was noted in any case where it had moved up or down behind the iris. In the last case (S. G.), the luxation was fairly complete, and for long years, the eye was free from irritation, and retained very good vision till the death of the child.

There are, however, some strange exceptions. I saw a patient in 1929, a clerk, in whom both lenses moved out into the anterior chamber every morning when he bent his head to wash his face: he could subsequently manipulate the lenses behind the pupil, by bending his head back. He says that he was more comfortable when the lenses were in the anterior chamber;



and actually saw better with his aphakic glasses which he generally used in his office. Ordinarily the lenses slipped back behind the pupil while he went to sleep. He had been working like this for a good few years, and had so far no trouble in his eyes. Srinivasan (1932) has reported two such cases of floating dislocation, but neither showed the same mobility as the case observed by me.

These cases are not easily amenable to treatment. They almost always have a certain extent of diplopia. The correcting lens, however, depends on the extent of the dislocation, and, as in the present case, may change radically with its progress. Extreme caution is advised in adopting any operative interference, and experienced operators such as Wright and Nayar say that they have seldom been successful in these operations. In these circumstances, the best course seems to be to give the most suitable lens, and watch and wait.

The handicap which this condition presents in life is great; with or without glasses, patients have never any satisfactory vision. The ultimate fate of a large number of these eyes is glaucoma, which has been described as the despair of ophthalmologists. Wright and Nayar have tried various surgical procedures for the relief of this glaucoma, but say that they seldom afforded relief: they add 'on the few occasions where a satisfactory immediate result was obtained, we feel that a sustained follow-up would reveal eventual failure'. Child N. P. in the present series of cases had an attack of secondary glaucoma in the left eye due to complete anterior dislocation of the lens. After the tension had been relieved, an attempt to remove the lens failed, and the subsequent history till the death of the child showed that there was progressive dimness of vision; this is in conformity with the experience of other observers.

I would consider it, therefore, very risky to submit the patient to a surgical interference in an attempt to remove a subluxated lens, even when there is no increased tension noted. It is a safer and, for the patient, a much better course to wait and watch and prescribe the most suitable glasses with which he can work. When however glaucoma supervenes, there is no other option but to interfere. It is best to obtain a temporary reduction of tension first and then attempt a removal of the lens; this becomes comparatively easy if the luxation is in the anterior chamber; otherwise it is a problem beset with the gravest difficulties and uncertainties.

It is proper to advise such patients to avoid parenthood, as the children will always remain at a great disadvantage in life, and very little can be done for the treatment of this condition. In countries where old customs and convictions die hard, I feel that it is more likely that in tendering this advice we may be expressing only a pious wish.

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## TREATMENT OF AN EPIDEMIC OF ACUTE BACILLARY DYSENTERY WITH M&B 693.

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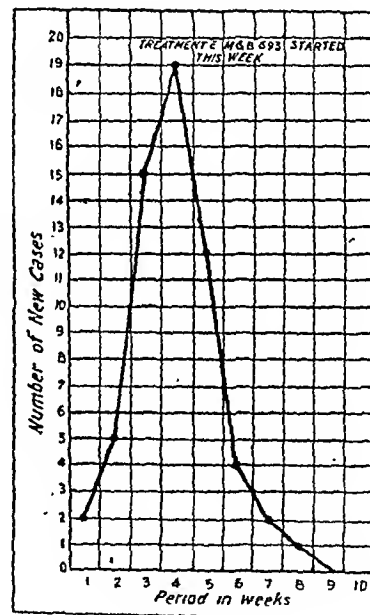
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An epidemic of acute bacillary dysentery occurred among the inmates of the Leprosy Hospital, Hendala, Ceylon, during the latter part of April, May and the early part of June 1943, during which period there were 60 cases. The results of treatment of this series are considered worth reporting because:—

1. Treatment was adopted at the same early stage in all cases, all the patients being under institutional control.

2. Treatment with serum and saline on the one hand and M&B 693 on the other was given in two sets of cases.

3. The results of treatment indicated clearly that M&B 693 was very efficacious in acute bacillary dysentery, effecting an almost complete cure in 3 days.



### Epidemiology

The epidemic started on 21st April. The first patient was a leprosy patient who was transferred from Mantivu on 18th April, 1943, and who developed dysentery on 21st April, 1943.

(Continued from previous column)

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The epidemic spread rapidly, with 2 cases in the 1st week, 5 in the 2nd week, 15 in the 3rd week, and reached its peak in the 4th week with 19 new cases. Thereafter the numbers declined, and there were only a total of 19 cases for the subsequent 4 weeks. The duration and the course of the epidemic suggest that it spread from case to case. Had it originated from infected milk or water, the numbers would have been much greater, and the peak would have been reached in the 1st week itself. Among the causes that tended to spread the disease were: (1) the 'fly season' at the time, (2) the aggregation of a large number of persons—there were about 650 patients in the hospital at the time, (3) the lowered resistance of the patients who were all suffering from leprosy, and (4) the difficulty of getting this class of patients to observe the rules of personal hygiene.

The rapid decline in the epidemic in the 4th week could be ascribed only to the rapid elimination of the sources of infection following the adoption of M&B 693 as treatment in the 3rd week, as the other factors remained unchanged.

The total number of cases was 60, which were distributed as follows according to age groups:—

Under 10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	Over 60 years
1	9	18	15	7	7	3

According to sex there were (a) males—44, (b) females—16.

**Clinical features.**—The symptoms and signs were typical. All the patients had frequency of stools—some over 30 motions a day—with almost pure blood and mucus, tenesmus, fever, and abdominal tenderness. Some patients showed a certain degree of toxæmia in spite of the fact that treatment was instituted early. The stools were inoffensive, and were composed of glairy mucus and blood. On microscopical examination they showed no amœbæ or cysts. The cell picture showed few red cells and a preponderance of polymorphonuclear leucocytes with a few macrophage cells. Bacteriological examination showed the causative organism to be *B. shiga* in the first two cases. No bacteriological examination was done in the other cases owing to difficulty of transport in sending specimens several miles away for examination, but the clinical features and the macroscopical and microscopical appearances of the stools suggested that the causative organism was similar in the other cases also.

**Treatment.**—The patients were treated on two different lines, viz, one set with serum and saline and the other with M&B 693. These cases were not selected alternately. The first few patients were treated on orthodox lines with serum injec-

tions and saline mixture four hourly, but some of them were getting worse and M&B 693 was tried on them. The rapid improvement of these encouraged further trials with this drug, and during the later part of the epidemic all the cases were treated with it.

(a) Cases treated with saline mixture and serum.

Forty-two patients were treated in this manner, of whom 18 were cured, giving a percentage of about 43. The period of treatment ranged from 5 to 18 days with an average of 9 days. But 24 cases forming 57 per cent did not improve, and some became worse and these were then put on M&B 693. All of them recovered in three days.

(b) Cases treated with M&B 693.

Eighteen patients were treated with M&B 693 from the beginning and all of them recovered in 3 days. The 24 patients who did not improve with serum treatment also recovered with 3 days' treatment with M&B 693. At the commencement, 18 pills (9 gm.) were administered as a course, 2 pills being given 3 times a day for 3 days. The dosage was later reduced in order to find out the minimum dosage that would be necessary to effect a cure. 12 to 15 pills were found to be sufficient in all cases. No cases of intolerance were noted with this dosage.

The following summary of the case histories of 3 patients is given to illustrate the clinical course of the illness and the efficacy of M&B 693:—

**Case 1.**—Tuan Ganny, male, 65 years, was admitted on 22nd May, 1943, with a history of having had 32 motions, all containing blood and mucus. He was given 4,000 units of antidyenteric serum immediately and was put on saline mixture 4 hourly. On the 23rd he had 24 motions and on the 25th he had 25 motions. Antidyenteric serum 4,000 units was repeated. He was getting worse and on the succeeding days he had 28, 35 and 30 motions. On the 28th he had 25 motions, and was very toxic and weak. He was put on M&B 693, 2 pills three times a day. The next day he had 9 motions and on the following day had only 5 motions. On 31st (i.e., 3rd day of M&B treatment) he had only one motion which was fairly well formed. The next 2 days he had no motions and was given liquid paraffin  $\frac{1}{2}$  oz. on 3rd day. He remained well.

**Case 2.**—John Perera, male, 50 years, was admitted on 15th May, 1943. He had 7 motions on admission with blood and mucus. He was given serum 4,000 units and put on saline mixture 4 hourly. Patient became steadily worse, having 15 and 20 motions respectively on the following 2 days. On the 18th, i.e. 3rd day, the number of stools could not be counted as he was passing them on his bedclothes. It was over 40, and patient appeared to be very bad. He was put on M&B 693—2 pills thrice daily. The next day, 19th May, 1943, he was definitely better and had only 10 motions. On the 20th he had only one motion which was formed. Since then the bowels were regular and stools formed and normal.

**Case 3.**—Louis Appu, male, 60 years, was a weak and debilitated patient who was admitted on 13th May, 1943, with a severe attack of dysentery. Had about 35 motions before admission. Was straightway put on M&B 693—2 pills thrice daily. The next day he had 15 motions and on the succeeding 2 days he was constipated and had to be given liquid paraffin to move the bowels. Since then the bowels were regular with formed stools.

TABLE I

Number, sex and age	Number of stools during the 24 hours prior to treatment	Dose of serum units	Number of days under serum and saline treatment	Results	PROGRESS OF THE UNCURED CASES UNDER M&B 693					
					Number of stools per day at com- mence- ment	Number of stools after one day's treatment	Number of stools after 2 days	Number of stools after 3 days	Number of stools on the 4th day	Number of M&B 693 pills adminis- tered
1, F., 50	5	..	7	C.	..	..	..	..	..	..
2, F., 36	9	..	7	C.	..	..	..	..	..	..
3, M., 30	10	..	5	C.	..	..	..	..	..	..
4, M., 35	6	..	4	C.	..	..	..	..	..	..
5, F., 70	10	..	9	C.	..	..	..	..	..	..
6, F., 40	18	8,000	18	C.	..	..	..	..	..	..
7, F., 29	18	4,000	14	C.	..	..	..	..	..	..
8, F., 20	8	4,000	8	C.	..	..	..	..	..	..
9, M., 35	5	8,000	14	C.	..	..	..	..	..	..
10, M., 40	8	4,000	5	C.	..	..	..	..	..	..
11, M., 15	12	8,000	6	C.	..	..	..	..	..	..
12, M., 35	4	4,000	5	C.	..	..	..	..	..	..
13, M., 24	7	4,000	8	C.	..	..	..	..	..	..
14, M., 26	10	4,000	8	C.	..	..	..	..	..	..
15, M., 16	8	4,000	7	C.	..	..	..	..	..	..
16, M., 25	20	4,000	6	C.	..	..	..	..	..	..
17, M., 50	15	4,000	16	C.	..	..	..	..	..	..
18, M., 33	12	8,000	15	C.	..	..	..	..	..	..
19, F., 30	7	..	5	N.I.	5	2	1	0	0	12
20, M., 55	7	..	8	N.I.	5	1	0	0	..	12
21, F., 16	20	4,000	6	N.I.	10	1	0	0	..	12
22, F., 24	20	4,000	16	N.I.	12	1	0	0	..	12
23, F., 8	16	4,000	14	N.I.	5	1	0	0	..	6
24, F., 20	16	4,000	6	N.I.	8	1	0	0	..	12
25, F., 35	10	..	3	N.I.	6	2	0	0	..	12
26, M., 35	7	..	3	Worse	25	1	0	2	1	15
27, F., 40	8	4,000	4	N.I.	8	3	1	0	..	12
28, F., 40	6	4,000	5	N.I.	8	2	0	1	..	12
29, F., 13	10	4,000	5	N.I.	6	0	1	0	0	12
30, M., 51	4	4,000	6	N.I.	6	0	0	1	..	12
31, M., 58	10	4,000	3	Worse	40	10	1	0	1	15
32, M., 30	15	4,000	7	N.I.	4	1	1	0	..	12
33, M., 36	10	4,000	7	N.I.	8	4	1	0	..	12
34, M., 28	8	4,000	7	N.I.	12	1	1	0	..	12
35, M., 23	10	4,000	5	Worse	20	2	2	1	0	12
36, M., 20	30	4,000	11	N.I.	6	1	1	0	..	12
37, M., 65	30	8,000	7	Worse	25	9	5	1	0	15
38, M., 45	17	4,000	14	N.I.	4	1	0	0	..	12
39, M., 48	20	4,000	10	N.I.	4	3	1	0	..	12
40, M., 60	20	4,000	11	N.I.	15	1	0	0	..	12
41, M., 60	20	4,000	10	N.I.	6	1	0	0	..	12
42, M., 25	10	4,000	4	Worse	20	4	2	0	..	12

C. = Cured. Stools formed and normal.

N.I. = Not improved. Stools loose with blood and mucus.

Worse = Number of stools increasing and general condition deteriorating.

*Deaths and relapses.*—There were no deaths and no relapses in the series. But it is very likely that the 5 patients (nos. 26, 31, 35, 37, and 42 in table I) who became definitely worse with serum treatment would have died had they not been changed over to M&B 693.

*Discussion.*—Opinion on the efficacy of serum in acute bacillary dysentery is divided. Graham (1918) stated that the mortality was reduced to 1 per cent in 200 cases in which serum was given. On the other hand, Macumber (1942), in a study of 237 cases of bacillary dysentery (not Shiga) in 52 per cent of which polyvalent anti-dysenteric serum was given, came to the conclusion that it could not be said that the use of serum materially benefited the group of

patients which was so treated. Acton and Knowles (1928) considered that serum was of value only in infections with Shiga's bacillus, and that it should be administered within 48 hours of the onset if it was to be of any use at all. In the present series, out of 42 cases treated with serum, only 18 were cured, giving a percentage of 43. The period of illness varied from 5 to 18 days with an average of 9 days. Fifty-seven per cent of the cases did not improve or showed very slow progress, and had to be treated with M&B 693 which effected a complete cure in 3 days. It is possible that some of these patients would have eventually recovered, but they would have done so only after a long debilitating illness. However in 5 cases the condition of the

patients was becoming progressively worse, and a fatal termination appeared highly probable when the administration of M&B 693 rapidly changed the prognosis.

On the other hand, all the 18 cases treated with M&B 693 from the beginning recovered in 3 days and the 24 failures with serum treatment

while serum treatment was being adopted, but with the adoption of M&B 693 in the 3rd week of the epidemic, the number of new cases began to decline rapidly and the epidemic died off in 3 weeks.

*Summary and conclusions.*—A review of 60 cases of bacillary dysentery in which treatment

TABLE II

Number, sex and age.	Number of stools at commencement of treatment	PROGRESS—NUMBER OF STOOLS PER DAY				Number of days under treatment	Number of pills
		1st day	2nd day	3rd day	4th day		
1, F., 35	24	5	3	2	1	4	18.
2, M., 21	7	0	0	1	..	3	18
3, M., 39	12	3	0	0	..	3	18
4, M., 52	9	5	0	0	..	3	15
5, M., 34	5	4	0	0	..	3	15
6, M., 18	14	3	0	0	..	3	14
7, M., 43	14	12	3	0	..	3	14
8, M., 22	20	12	4	0	..	2	12
9, M., 22	15	10	4	0	..	2	12
10, M., 16	6	0	0	1	..	2	10
11, M., 26	24	9	4	0	..	2	12
12, M., 75	22	5	5	1	0	2	12
13, M., 60	30	15	0	0	1	2	12
14, F., 35	12	5	0	0	..	2	12
15, M., 29	8	6	0	1	..	2	9
16, M., 50	20	5	0	0	..	2	9.
17, M., 24	20	10	4	1	..	2	9.
18, M., 48	12	1	0	0	..	2	9.

also recovered in 3 days, giving 100 per cent cures. Reitler and Marberg (1941) in a study of 20 cases reported that the treatment of bacillary dysentery with sulphapyridine had proved with them to be highly efficient, and that after 48 hours' treatment the motions were back to normal in nearly all cases, irrespective of the duration of the disease and the type of the dysentery bacillus. They gave 1 gm. (2 tablets) by mouth 3 or 4 times daily for 2 to 4 days (together with sodium bicarbonate to avoid nausea). Bell (1941) treated 16 cases with 0.5 gm. (1 tablet) M&B 693 4 hourly by mouth and reported that the results obtained were very satisfactory and that in all cases the symptoms cleared up in 36 to 72 hours. The average total amount given by him to each patient was 5 gm. (10 tablets). Compton (1943) in a comparative estimate of the value of phage, sulphaguanidine and sulphapyridine in acute bacillary dysentery showed that sulphapyridine appeared to be the more efficient of the two sulphonamides and that the time taken to bring down the stools to 2 or less per day was 3.0 days with sulphapyridine, 3.1 days with phage and 5.3 days with sulphaguanidine.

M&B 693 would thus appear to be a very potent drug in the treatment of bacillary dysentery, and the complete and rapid cure of this disease would be of very great value in tropical countries where epidemics of bacillary dysentery are frequently encountered. From the graph on page 117 it would be seen that the number of fresh cases was steadily increasing

with serum and M&B 693 were tried in 2 groups is given. From this it is submitted that the following conclusions may be reasonably drawn:—

1. That 12 to 15 pills (6 to 7½ gm.) of M&B 693 effect 100 per cent clinical cure in cases of bacillary dysentery.
2. That it reduces the period of illness to 3 days.
3. That it costs far less than serum treatment, considering the cost of serum and the cutting down of the period of hospitalization.
4. That it avoids the pain of injections of large doses of serum and the possible risk of anaphylactic phenomena.
5. That it would help to stamp out epidemics very quickly by the rapid cure of the cases, thus eliminating the sources of infection.

I wish to express my thanks to Dr. P. B. Fernando, professor of medicine, University of Ceylon, for his very valuable help and guidance in the preparation of this article, and to Dr. D. S. de Simon, medical superintendent, Leprosy Hospital, Hendala, for his encouragement and for supplying M&B 693.

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# HIGHLY POTENT WHOLE LIVER EXTRACT

HG %	RSC count
100	5
90	4.5
80	4
70	3.5
60	
50	
40	
30	



2cc. 2cc. 2cc. 2cc. 2cc.



FOR THE  
TREATMENT  
OF  
PRIMARY  
AND  
SECONDARY  
ANAEMIAS

**CIPALON**  
FOR PARENTERAL USE  
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## The Non-toxic Anthelmintic

Diphenan, p-benzyl-phenyl carbamate, formerly only obtainable from Germany under a proprietary name, is a synthetic substance which, over a period of several years, has been increasingly used for the treatment of threadworm infestation. Diphenan has distinct advantages over the substances previously used in that the incidence of reactions produced in the patient is considerably lower and the few symptoms produced are markedly less disturbing and of no permanent significance.

Such symptoms as nausea, xanthopsia and other visual disturbances which are produced by santonin are not produced by diphenan, and it may safely be given to patients known to be intolerant to santonin.

Diphenan B.D.H. is an exceptionally highly-purified substance which, on oral administration, rapidly brings about extreme contraction of the parasite and prevents deposit of eggs; it can be relied upon to produce uniformly successful results.

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# Indian Medical Gazette

MARCH

## STILL ANOTHER METHOD OF STAINING MALARIA PARASITES

In our last number we published an editorial note emphasizing the importance of rapid methods of staining malaria parasites in order to attain greater accuracy in the diagnosis of malaria and greater economy in the use of the limited supplies of quinine available. The method specially discussed in that editorial was that of Field which is applicable mainly to thick films, and we strongly recommended the wide adoption of that or similar methods. These stains have the advantage of not necessitating the use of methyl alcohol or of the special stains which are now limited in supply and very expensive.

In our present number we publish an article by Major Jaswant Singh and Dr. L. M. Bhattacharji of the Malaria Institute of India. This article describes a method of preparing from ordinary methylene blue and eosin a water soluble stain which can be applied to thick films, and also to thin films after fixation with one or two drops of methyl alcohol. The authors sent a specimen of this stain for us to test, and we have done so with most excellent results. We have also prepared the stain according to their directions, and while we did encounter a few difficulties in the preparation of the stain, we have been able to overcome these difficulties and to produce a stain which gives results which these authors describe. So far we have had no very satisfactory substitute method of staining thin films. This new method can be recommended.

We feel that these methods of staining are not mere war-time substitutes for Leishman's stain and Giemsa stain, but that they have certain practical advantages over these classical stains. They are much more rapid and also in many ways much more simple; they do not tend to go wrong so easily with some little variation in the time of staining or in the reaction of the water, and so on. We believe that these stains, or some modification of them, have come to stay, and that they make blood examination for malaria parasites much more widely practicable than the older methods.

J. L.

## THE PROBLEM OF VITAMIN A DEFICIENCY

In recent years it has become increasingly clear that vitamin A deficiency is very common in India. The most important result of vitamin

A deficiency is blindness produced by xerophthalmia. Ophthalmologists state that there are at least two million blind persons in this country, and a large proportion of this blindness could have been prevented by the timely administration of products rich in vitamin A. The editor will never forget the day when in a certain town in western India on one day at one clinic he saw over one hundred severe cases of xerophthalmia, in most of which blindness was inevitable.

But xerophthalmia is only the most serious result of vitamin A deficiency. Diet surveys in various provinces have revealed the fact that almost everywhere the intake of this vitamin is lower than it should be. Thus it was found in South India that the diet of children in various hostels may contain as little as .68 mgm. of carotene (provitamin A) per day, whereas 2 or 3 times this amount is really needed. The application of dark adaptation tests has also revealed widespread deficiency in India, and stress is now being laid on the importance of augmenting the daily supply of vitamin A.

Indian diets are generally poor in animal fat, and the chief source of vitamin A is green vegetables containing the pigment carotene which is converted within the body into vitamin A. Most vegetables are taken cooked, and the small amount of provitamin present is considerably reduced by the processes of cooking. It is moreover a curious fact that the intake of green vegetables is very often inversely proportional to the income of the family so that vitamin A deficiency is not confined to the poor. Well-to-do people take more milk and ghee and these are their chief sources of vitamin A; but they are not very good sources, and thus even well-to-do people often suffer from vitamin A deficiency.

Before the war, imported cod liver oil had a big market in India for those who could afford it, and this is of course rich in vitamin A. Now this imported supply has practically ceased. Recently some attention has been paid in India to shark liver oil which is very rich in vitamin A, and it is understood that supplies are now available from the Madras and Travancore Fishery Department. The quantity however is small compared with the population of India even if they could afford to buy it and be persuaded to take it. In India many people are vegetarians and will not take such products.

It is therefore highly desirable that adequate supplies of vitamin A of high potency prepared from vegetable sources should be made available. It is also desirable that such a product should be prepared so that its taste is not unpleasant and so that it can be incorporated into commonly used edible fats. There is a large demand for this vitamin for the army, and also by certain sections of the general population who are alive to the needs.

In our present number we publish an article from the Imperial Veterinary Research Institute. This article discusses the production from vegetable sources, of a product very rich in



vitamin A. This material can be incorporated into vegetable fats to give the same level of vitamin A potency as that found in natural butter.

One interesting point reported by the authors is that the tender leaves of water hyacinth forms a very rich source of carotene. This plant occurs

in many parts of India and the leaves are available for nothing or next to nothing. If out of water hyacinth there can come an adequate supply of a vitamin A preparation suitable for wide use in India, then good will indeed have come out of evil.

J. L.

## Medical News

### BOOTS PURE DRUG COMPANY, LIMITED

It is reported that a gift of one million halibut liver oil capsules has been made by Boots Pure Drug Company, Limited, manufacturing chemists, Nottingham, England, for the benefit of medical relief in Bengal.

### DIPLOMA IN CHILD HEALTH (D.C.H. Bom.)

THE Council of the College of Physicians and Surgeons of Bombay, at its meeting held in July 1943, decided to institute an examination for a diploma in child health and appointed a committee to draw up regulations for that examination. The committee submitted its report to the meeting of the council on 14th January, 1944. The report was approved and adopted.

The course, which is of twelve months' duration, has to be taken at a recognized children's hospital or in a recognized children's department of a general hospital. The examination is open to persons holding a qualification: (a) laid down in Schedules I and II of the Indian Medical Council Act, 1933, or (b) granted by any of the various examining boards in India whose names were on the Schedule of the Bombay Medical Council in 1941.

### OFFICIAL STANDARDS FOR INDIAN DRUGS: DRUGS TECHNICAL ADVISORY BOARD TO PREPARE LIST

THE Government of India have entrusted to the Drugs Technical Advisory Board established under the Drugs Act, 1940, the task of preparing an Indian Pharmacopoeial List.

There are a number of drugs of Indian origin which are of sufficient medicinal value to be officially recognized and which are prescribed in India by practitioners of modern scientific medicine but which are not included in the British Pharmacopoeia. Pharmacopoeial drugs are also produced in India from medicinal plants of a slightly different species from those described as standard in the British Pharmacopoeia. It is necessary to prescribe official standards for such drugs in order to secure uniformity of strength, quality and purity.

The Indian Pharmacopoeial List will be the official standard for drugs not included in the British Pharmacopoeia and will serve as the official supplement to the British Pharmacopoeia. In preparing the List the Board will have the advantage of the considerable material collected as a result of the enquiry into indigenous drugs conducted over a period of years under Lieut.-Colonel Sir R. N. Chopra.

### INDIAN MEDICAL COUNCIL

In exercise of the power conferred by clause (a) of sub-section (1) of section 3 of the Indian Medical Council Act, 1938 (XXVII of 1933), the Central Government is pleased to nominate Lieut.-Colonel Jelal M. Shah, O.B.E., I.M.S. (Retd.), to be a member of the Medical Council of India, from Bombay, with effect from the 9th February, 1944, *vice* Dr. Jivraj N. Mehta.

### MEDICAL RESULTS IN THE TUNISIAN CAMPAIGN\*

THE treatment of the British wounded in the Tunisian campaign seems to have been the most successful recorded in war. This result can partly be explained by the innovation of transport by air. Toward the end of the previous great war one British hospital in France had 1,300 severely wounded, of whom 113 died. In Tunis a similar hospital had 1,500 severely wounded, of whom only 5 died. Full statistics are not yet available, but we are assured that when they are they will amaze the world. There has been no tetanus and little gas gangrene, and sepsis has been largely controlled by sulphonamides. These results have been achieved in spite of great transport difficulties. The wounded had to be moved hundreds of miles, sometimes by motor ambulance, sometimes by hospital train. Once we gained air superiority it was possible to send them by hospital ship. But the most valuable means of transport were troop carrier aircraft fitted to take 18 stretcher cases, as well as air crew, doctor and nurses. More than 15,000 wounded were evacuated by air, usually to Algiers or Oran, sometimes to Gibraltar, occasionally even to America or England. In April alone 7,000 were thus transported. Aircraft also carried medical supplies in the opposite direction. One flew plasma to the Eighth Army in Tripoli. The most remarkable achievement was to fly the whole of a small general hospital to American troops isolated in desert country. The job took eighty loads, but it was done in one day.

The lives of many wounded in Tunisia were saved by blood transfusion and many more by major operations performed closer to the firing line than ever before. Our new field surgical units, staffed by young surgeons, have done miracles under fire. The air borne surgical team proved worthy of the parachutists whom it served and with whom it dropped. One surgeon broke his leg above the knee in landing. He concealed the injury for three weeks during which he performed a number of major operations, giving himself a local anaesthetic between operations. Another hid a severe wound for thirty-one hours.

The general health of the First Army was no less remarkable than its recovery from wounds. Probably no force on active service has ever been healthier. The much disliked inoculations produced complete absence of tetanus and almost complete absence of typhoid. There were hardly any typhus cases, though there was much typhus in the country and there was a severe epidemic during the previous winter. The malaria season began last month, but plans to control the disease were begun in January. All the troops now take anti-malaria pills, which they dislike very much.

\* Abstracted from *The Journal of the American Medical Association*, 17th July, 1943. Vol. CXXII, p. 823.

### CORRIGENDUM

In the article entitled 'A clinical study of fifty cases of meningo-vascular syphilis' by B. K. Ramakrishna Rao, published in the January 1944 number of the *Gazette*, on page 33, left hand column, the third line from the top should read 'found changes in the fundus in only four cases'.

## Public Health Section

RESULTS OF A SURVEY UNDERTAKEN  
IN A RURAL AREA IN BENGAL IN  
MATERNITY AND CHILD WELFARE

By LEILA GHOSH

and

C. CHANDRA SEKAR

*(All-India Institute of Hygiene and Public Health)*

IN common with all personal health service, the efficacy of maternal and child welfare work in protecting mothers and infants is largely dependent upon the conviction of the public that direct benefit will accrue to the individual from utilizing the facilities offered.

This outlook is a natural one and deserves thoughtful consideration. Time has to be spared by the pregnant woman or mother from domestic duties to attend a prenatal or infant clinic. To ensure regular attendance, which is the only calculable safeguard of health, the woman, her husband, and perhaps mother-in-law also, must be made to feel that her regular absence from the house, the time expended and, in a rural area, the discomfort of a walk of perhaps two miles or more each way, whatever the weather, are compensated for by the benefit derived from the visits. This means that even the crudest programme must meet the important needs of the woman, be they for maintenance of health or for control of abnormality. Lack of institutional facilities can therefore nullify the effects of an otherwise efficient scheme. By the public, in the early stages of a programme at least, success is not judged by the normal cases better cared for, but by the abnormal cases well handled. In maternal and infant care, it is on this platform that care and prevention meet, and review of facilities must include review of the local provision for treatment, therapeutic or obstetrical.

For this reason, from the administrator's point of view, before a scheme is drawn up or further developments in an existing scheme are considered, these needs must be ascertained. This is particularly true of an Indian rural area, for not only are the funds available for maternity and child welfare work likely to be small and so require careful expenditure, but the standards of education, social habits, communications and medical facilities may vary so widely within a distance of ten miles that the programme destined for area 'A' may leave the people of area 'B' entirely unresponsive. The programme to make 'touch' must be realistic.

The study of relatively small rural populations, e.g. of the size of the Union Board in Bengal (10,000 to 15,000 population), therefore commends itself to the administrator responsible for the planning of a programme in maternal and infant care. The figures on which such a

plan would be based might however be much too small to satisfy the statistician when the question arises of assessing improvement effected by the maternity and child welfare service year by year. This raises a question of no small significance.

It is open to consideration whether, in order to obtain assessment satisfactory to the statistician without the rates having to refer to populations of over  $1\frac{1}{2}$  lakhs (and therefore consisting of many units of population of diverse habits and outlook), negative indices, such as mortality rates, might not be considered in conjunction with positive indices of health improvement such as are obtainable from records of development of the infant.

If this combined assessment can be applied to smaller units of population, with less likelihood of error, then there is common ground upon which administrator and statistician may meet to reduce the essential size of a unit population for maternity and infant welfare planning. The present study presents chiefly the administrator's point of view, as no data relating to development of the infant during the period studied were available.

Upon these considerations, the problem of planning a programme resolves itself into two parts:

I. To collect as accurately as possible the minimum information relating to the area, which will disclose the major lags in the care of pregnant women, post-delivery cases and infants. This information will be under three heads: (a) general information upon topography, communications, sociological conditions and facilities for maternal and infant welfare and (b) information regarding vital occurrences, (c) data relating to development of the infant if available.

II. To use the information as a guide in planning.

In May 1942, an approach to the problem on these lines was made by the Department of Maternity and Child Welfare of this Institute when, on the invitation of the local authorities, it was proposed to initiate welfare work in the Union of Tarakeshwar, Hooghly District, Bengal.

To supply information I (a), a map of the area 4 inches to 1 mile was obtained, and the District Board was asked to supply the population figures for the villages derived from the 1941 census. Topographical and sociological data were collected by the staff during talks with members of the Union Board and from observations made in the villages and homes while obtaining information relating to vital occurrences.

In regard to information I (b), it was decided that data upon the following points should be collected:—

1. How many women became pregnant in the area within a recent twelve-month period?
2. How many of these pregnancies terminated with viable births, live or still?
3. Where did the deliveries take place?
4. Who conducted them?
5. How many deliveries were attended by complications, who dealt with the complications, and with what result?

6. How many live born infants survived for one year?
7. How many mothers did not survive delivery by three months?
8. What were the known causes of infant and maternal death?
9. What proportion of the live births were registered and to what extent was birth registration complete?
10. To what extent was infant and maternal death registration complete?

Where an efficient system of birth and death registration is in operation, reliable information on items 6, 7 and 8 would be available from the registers. On the other hand, under an existent maternity and child-welfare scheme, if all pregnant women have been contacted early and recorded, and systematically followed up throughout pregnancy and for three months after delivery, and if the infant is kept under observation for a year from birth, references to the prenatal and infant cards of the centre would supply all data relating to items 1 to 8.

If neither of these sources can be utilized, as was the case in the present instance, only one method of collection remains, namely inquiry in the homes; i.e. a form of survey, supplemented by checking of the data collected, with the entries in the birth and death registers.

Regarding the development of the infants, no data were available as no infant welfare service had been in operation.

The following statistical considerations have to be borne in mind :—

By obtaining information of every pregnancy in the area, true figures for the surveyed population for the period under investigation can no doubt be secured so that the rates based on the figures give the correct picture for that period. The administrator is, however, not interested only in what can occur in any one year but also in the possible upper and lower limit for the important rates and other indices. If it is elicited that the percentage of infant deaths occurring before one month of life is 70 in one year, is it safe to assume that under existing conditions this percentage in another year will not fall below 40?

If the natural conditions give an equal chance to every infant to survive any period during the first year of life, then the result of the survey can be compared to the proportion of black and white balls withdrawn each time when an equal number is abstracted from a bag containing a large number of black and white balls of equal size. The variation in proportion of black and white balls in the sample is subject to the law of chance and so would also be the neonatal and infant mortality rates obtained during the survey. Is it justifiable to assume that every infant or group of infants runs the same risk? Presumably not, because of biological and other variations not strictly comparable to chance happenings.

A study of vital occurrences in other communities over a succession of years may offer a clue to the solution; yet it will not do so fully. As a working hypothesis it appears that the theory of chance can be used in the manner explained above for inductive purposes. According to this theory, the range of variation of a proportion depends (1) upon the number of observations on which it is estimated and (2) upon the magnitude of the proportion. The exact lower and upper limits can be obtained by using the charts provided by Clonner and Pearson (1934). Approximate values can be obtained by adding to, or subtracting from, the proportion 'p' obtained from the survey  $1.96$

$\sqrt{p(1-p)}$  where 'n' is the number of observations

from which 'p' is obtained. The larger the number of observations, the smaller the range. The more the proportion deviates from unity towards zero, the longer the range as contrasted with the magnitude of the proportion. This shows that in general greater reliance can be placed on infant mortality rates than on the

proportionate mortality within a month as the former is based on a much larger number of observations. Similarly, though the maternal and infant mortality rates are based on much the same number of observations, the maternal mortality is less reliable as maternal mortality rates are much lower than infant mortality rates.

### I. (a) General data

Tarakeshwar Union covers an area of approximately  $7\frac{1}{2}$  square miles and comprises 24 villages, predominantly Hindu, formed into 19 areas of village administration. Excluding the villages of Teghari and Gouribati, for which no figures could be obtained, the population of the area as estimated at the 1941 census was 13,714.

Except in one particular, the area is typical of rural Bengal. The Union includes the market 'town' of Tarakeshwar, a renowned place of Hindu pilgrimage, with a population of over 4,000 inhabitants. Whereas elsewhere the residents are agriculturists, on the whole, very poor, in Tarakeshwar the bulk of the population consists of moderately well-to-do shopkeepers and others associated with, or catering for, the religious establishment which owns lands in 13 of the villages of the Union. Of the 9 medical practitioners who practise in the area, 4 reside in Tarakeshwar. The only hospital in the Union is maintained by the Estate of the Endowment, and although four beds are reserved for women, no provision for maternity work exists, nor is there a woman doctor stationed, or practising, in the area. The Hooghly District Board maintains a free dispensary at Loknath. This village, a small one near the south-eastern extremity of the Union, about  $1\frac{1}{2}$  miles from Tarakeshwar, was the headquarters of the staff during the survey.

As can be seen from the map, the railway from Calcutta terminates at Tarakeshwar and so does not run through more than a small part of the Union; from Calcutta the journey of 30 miles takes  $2\frac{1}{2}$  hours. It is to Calcutta that maternity and other cases are taken if necessary; the small hospital at Singur, the larger one at Serampur and the maternity home attached to the Singur Health Unit, although nearer, are little patronized by residents of the Tarakeshwar Union.

Most villages of the Union are accessible from Tarakeshwar, but by rough paths only, in many cases passing through or between the fields. Journeys have to be made on foot or by bullock cart, and in many cases to reach the further villages takes two hours or more. The main road is negotiable by taxi or bicycle only in the dry weather. As it is deeply rutted by bullock cart wheels, even at the best season, these methods of conveyance are associated with considerable discomfort and some danger.

Apart from Tarakeshwar, three of the villages of the Union have a population exceeding one thousand, and seven have fewer than five hundred inhabitants. From Loknath the furthest village is about four miles distant, but the majority of the villages lie within a radius of 2 to  $2\frac{1}{2}$  miles.

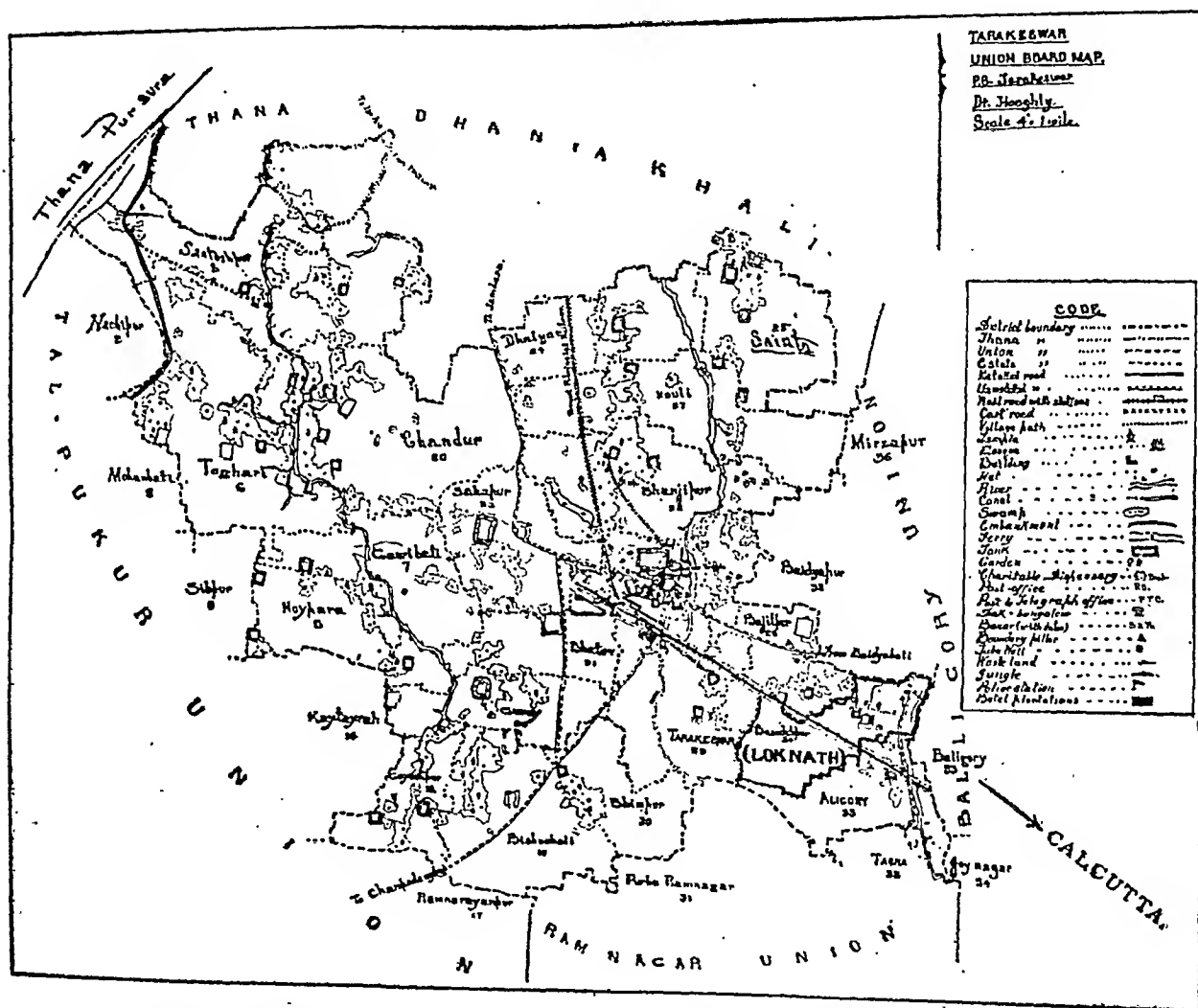
Only during the latter part of the survey was a small bullock cart used by the staff as a means of transport.

Under such circumstances, data for the entire area were collected during the months of November and December in a period of under six weeks allowing five and half working days a week, by two teams each consisting of a health visitor and a midwife. The total cost of the survey, inclusive of salaries, rental of quarters and transport charges, did not exceed Rs. 730.

Through the courtesy of the Union Board, the sanitary engineer, the members of the police

the village or villages comprising his 'beat'. The method employed is for the chowkidar to make the entries once a week in the appropriate *hatchitta* or register maintained in the office of the President of the Union Board (which is usually in the village of which the President is a resident). Separate registers are maintained for births and deaths, and the dates are recorded in accordance with the Roman Calendar. In the case of three villages, Santoshpur (population 1,288), Santa (population 388) and Jotshmali no birth *hatchittas* were available for the period covering 1940, 1941 and 1942.

MAP



force, and the chowkidars were introduced to the Senior Health Visitor, and the *hatchittas* or local birth and death registers were made available for scrutiny.

(b) *Data relating to vital occurrences*

*Method of registration of births and deaths.*—In the Union, 17 chowkidars are employed by Government, on a salary of Rs. 6 per mensem, and among other duties, each chowkidar is responsible for the collection and recording (usually in Bengali) of all births and deaths in

From the *hatchittas*, lists were made of the births and the infant and maternal deaths occurring during the three years 1940 to 1942, in order to allow for discrepancies in the dates as registered and as elicited, when checking. The period for which information was collected was (1) for births, 1st July, 1940 to 30th June, 1941, (2) for infant deaths (to permit each infant to attain one year of age), 1st July, 1940 to 30th June, 1942, (3) for maternal deaths (to include deaths up to three months after delivery), 1st July, 1940 to 30th September, 1941.

The programme of work was as follows:—

Monday to Friday :

8 a.m. to 2 p.m.	House to house visits.
4 p.m. to 5-30 p.m.	Scrutiny of the day's schedules, converting of dates from the Bengali to the Roman Calendar and checking against the lists of births and deaths.

Saturday :

9 a.m. to 12 noon.	Final check and record of the week's schedule. Repeated visits to any village if the information required checking or supplementing by a second house visit.
--------------------	--

Unless the village was a very small one, requiring only one team, both teams visited the same village, accompanied by a local man as guide, and usually also by the chowkidar of the village, who was always informed in advance of the visit. In the house not only were the male and female adult members questioned regarding births and deaths during these intervals, but all the children in the home were seen, so that no living child between the ages of 16 and 22 months was likely to be missed. Dates of births and deaths were recorded, as given by the householder, according to the Bengali Calendar, as it was felt that greater accuracy could be obtained in this way.

These visits attracted so much interest on the part of the men, women and children that corroboration or correction of the information given by the householder was almost always forthcoming from the neighbours, who cheerfully followed the team into the house. In almost all cases information was readily given and many questions were asked regarding the object of the survey.

Births and deaths found on the registration list but not detected during the house to house inquiry were discussed with the chowkidar, and often a return visit to the village was paid to check the discrepancies.

As the head of the section accompanied the teams on several visits, it was possible to obtain a rough estimate of the physical condition of women pregnant at the time of survey also, and to note the prevalence of symptoms of dietetic deficiency. Angular stomatitis, photophobia and bisymmetrical pigmented patches on the face, evidence of deficiency of vitamin B<sub>2</sub> and nicotinic acid, were commonly encountered amongst women of child-bearing age, pregnant women and young children. Eye disease was not very conspicuous. Although, habitually little milk or milk products are consumed in any but well-to-do homes (the milk is usually converted into *channa* and sent to Calcutta for sale), little ocular evidence of vitamin-A deficiency was detected, but from the prevalence of pyorrhœa and bleeding gums, vitamin-A and vitamin-C deficiency could be adduced. The diet in most houses consisted of rice and dal, sag and potato taken twice daily cooked in mustard oil. Fish and curd are in some houses

eaten once or twice a week. *Dhab* is not readily obtainable in this area. The chief crops are rice, grams, potato, sag and to a less extent onion, although all greens grow well.

The information elicited was therefore as far as possible complete. A type schedule is given in the Appendix and is so drawn as to facilitate the analysis of data by mechanical tabulation.

*Findings.*—During the twelve months studied, 448 pregnancies were recorded; of these 2 terminated as abortion, and 5 as twin births. In the case of one pair of twins, record of only one infant was available. The twin-birth rate is thus 1 per cent (approximate) and similar to the urban rate. All viable births amounted to 450, of which 2 were still births. Twenty premature births were reported. In one case diagnosis of maturity was not possible.

The 488 pregnancies thus yielded 0.4 per cent abortion, 4.5 per cent premature birth, and 95.1 per cent full-term live birth. The still-birth rate was 44 per 1,000 live and still births. Similar figures for Calcutta are abortions 2.6 per cent, premature birth 8.9 per cent, full-term live birth 87.6 per cent, still-birth rate 40 per 1,000 live and still births.

*Nature of the delivery.*—Of the 446 women in whom the pregnancy terminated with a viable infant (in five instances it was not known whether or not interference was resorted to), 435 (98.6 per cent) were found to have been delivered without skilled interference. Among the remaining 6 cases, in 5 cases forceps were applied and in 1 case craniotomy was performed.

These 6 cases were conducted in a maternity hospital in Calcutta.

*Place of delivery.*—Considering only women resident in the villages, of 412 cases in which pregnancy terminated after the 28th week, 401 (97.3 per cent) deliveries took place in a house (in the village or elsewhere) and 11 (2.7 per cent) in an institution.

*Agent of delivery.*—In certain respects, the circumstances attending births in Tarakeshwar differed from those associated with births elsewhere in the Union. It is not an uncommon practice for orthodox Hindu families (not only of Bengal, but many of other provinces who are resident in Calcutta) to visit a relative or to rent a house in Tarakeshwar, so that the birth may take place under favourable auspices. The period of stay after delivery in such cases varies, but record of the child for one year after birth was in one case impossible to obtain. In the schedule this was recorded as 'contact lost'. Visitors of such a type do not conform to the customs observed in the area for maternity or infant care and this difference is reflected in the choice of agent at delivery and in registration of the birth.

For these reasons, the returns for Tarakeshwar require to be considered separately.

For the whole Union (excluding Tarakeshwar) the reported agent of delivery at 374 viable terminations of pregnancy was as follows: not



known, 3; 'no one', 214; 'relative', 2; 'dai', 149; 'midwife', 1; 'doctor', 5.

For Tarakeshwar the returns for 72 viable terminations were 'no one', 2; 'relative', 24; 'dai', 35; 'midwife', 7; 'doctor', 4.

Expressed as percentages these returns can be readily compared.

Agent of delivery	The Union excluding Tarakeshwar	Tarakeshwar
Doctor ..	1.3%	5.6%
Midwife ..	0.3%	9.7%
Dai ..	40.1%	48.6%
Relative ..	0.6%	33.3%
No one ..	57.7%	2.8%

The differences in custom and social outlook are clearly seen from the figures. Whereas in the whole area, excluding Tarakeshwar, in 57.7 per cent of cases no one attended the woman at the time of delivery (often not even to cut the cord after the birth), for Tarakeshwar, the corresponding figure is only 2.8 per cent. While in Tarakeshwar over 15 per cent of cases were attended by a doctor or midwife, the corresponding figure for the Union is 1.6 per cent.

The attitude adopted generally in the area is that delivery is an affair for the woman herself and that except in special circumstances no assistance is called for. The woman shortly after delivery is expected to go to the nearest pond, wade into the water to bathe herself and to wash her clothing and soiled linen, in order to avoid polluting the house. The infant as a rule is not bathed for a week after birth. In general, *dais* when summoned are wanted only after the delivery, to cut the cord, and their services are not usually sought to make the woman comfortable or to give her any form of simple postnatal nursing care. To what extent poverty has influenced this custom is not clear; it is certainly not now restricted to the poor.

It will be seen that whereas in Tarakeshwar in 48.6 per cent of deliveries a *dai* attended, in the rest of the Union in 40.1 per cent *dai* was sent for, in most cases only to cut the cord.

The social ostracism of the woman in labour by the general population is seen in the figure for 'assistance by a relative'—against 33.3 per cent in Tarakeshwar it is 0.6 per cent for the rest of the Union.

It is of interest to note that a similar survey in 2 large villages of the Singur Health Unit, not much more than 10 miles away, yielded a high figure for delivery by relative. The diversity in habit from locality could not be better demonstrated.

**Birth rate.**—Excluding the villages for which no population figures were available, but including Tarakeshwar (where the proportion of women to men is very much lower than elsewhere—37.7 : 62.3 against 48.3 : 51.7, giving a

general proportion for the area of 44.9 : 55.1) the birth rates of the area were :—

*Calculated from collected data :—*

Resident birth rate .. 26.9 per mille  
Crude birth rate .. 27.5 per mille

Excluding Tarakeshwar, the rates are :

Resident birth rate .. 33.2 per mille  
Crude birth rate .. 34.1 per mille

**Infant deaths.**—Of the 448 infants known to have been born alive, contact was lost with one only before one year was attained, and 38 were known to have died during the first twelve months of life.

This yields an infant mortality rate of 85.0 per mille. Of these deaths, 17 (44.7 per cent) occurred within the first week of life, 9 (23.7 per cent) between a week and a month, which makes the proportionate death rate within the first month of life 26 (68 per cent), an extremely high figure.

However between the ages of one and three months, 3 infants died, and between three and six months 2 infants died. Seven deaths occurred between six months and one year, three (7.9 per cent) between six and nine months and four (10.5 per cent) between nine months and one year. In the table below are shown the 38 elicited infant deaths distributed by age periods according to the ascribed cause of death or associated conditions.

**Maternal deaths.**—Only 2 maternal deaths were reported to have taken place in the area : this gives a maternal mortality rate of 4.4 from 1,000 pregnancies or 4.4 per 1,000 live births.

**Registration.**—Birth registration is compulsory within 8 days of birth in the registration area of Bengal. As a means of providing information of births for early contact of the infant by the health staff, birth registration is of great importance; it also offers a guide to the number and distribution of live births upon which estimates of the staff needed and other details of programme must be based. No general principle of ratio or number of health visitors to population can be applied in rural areas in India as long as conditions are so variable, unless superficial service only is planned.

Lists of registered births were available for 16 of the 19 village administrations of the Union. In the case of two large adjoining villages, Teghari and Santoshpur, no *hatchitta* could be traced.

The birth lists covered 320 births of which 120 (37.5 per cent) were registered. It is not impossible that a few registered births were lost due to incorrect entries in the *hatchittas* attributable to the illiteracy of the chowkidar. For 100 births (in Teghari and Santoshpur) no registration lists were available upon inquiry from either the Union or District Boards. To residents in villages for which registration lists were available there were 23 births recorded as



taking place outside the village; of these, 2 were registered.

To residents of villages for which *hatchittas* were not available, out of 5 births known to have taken place outside the village, 1 was registered to our knowledge. Of the total 123 registered

*Death registration.*—No special places or ghats are reserved in the villages for the disposal of the dead, and the chowkidar may learn of the death long after the event. In the case of infants, death is particularly likely to be unrecorded. In 11 cases, known infant deaths were

#### Number of infant deaths

Cause of death	Within a week from birth	Between 1 week and 1 month	Between 1 and 3 months	Between 3 and 6 months	Between 6 months and 1 year	Total
1. Not known .. ..	9	4	2	Nil	5	20
2. Pneumonia .. ..	Nil	Nil	Nil	1	1	2
3. Tetanus .. ..	1	2	1	Nil	Nil	4
4. Congenital debility ..	Nil	1	Nil	Nil	Nil	1
5. Septic umbilicus ..	1	Nil	Nil	Nil	Nil	1
Death associated with						
1. Dystocia .. ..	2	Nil	Nil	Nil	Nil	2
2. Premature delivery ..	4	Nil	Nil	Nil	Nil	4
3. Diarrhoea .. ..	Nil	1	Nil	Nil	Nil	1
4. Fever .. ..	Nil	Nil	Nil	1	Nil	1
5. Fever and chill ..	Nil	1	Nil	Nil	Nil	1
6. Marasmus .. ..	Nil	Nil	Nil	Nil	1	1
Total ..	17	9	3	2	7	38

and known births, in 42 instances (34.1 per cent) the elicited date birth agreed exactly with the date as registered. In 19 cases (15.4 per cent) the date as registered *anticipated the elicited date*, while in 62 cases (50.4 per cent) the birth, when compared with the date of birth as elicited, was post-dated in the register.

The degree of discrepancy between the dates can be seen from the following table in which the ante-dated and post-dated cases are divided according to the periods of discrepancy.

found registered. Of the thirty-eight deaths elicited, in 3 cases the death was of an infant whose mother had come to the house of a relative in the village, for delivery. For 3 villages no death *hatchitta* was available. The percentage of registration of death was 30.5. Of the eleven deaths registered, in 10 cases the information regarding date of death tallied with that elicited in the house.

*Discussion.*—Much greater care is necessary in the recording of vital occurrences—the limita-

#### Period of discrepancy

Date of birth in the register	Less than 1 week	1 week to 1 month	1 to 3 months	3 to 6 months	6 months
Ante-dated ..	57.9%	26.3%	15.8%	..	..
Post-dated ..	29.0%	37.1%	19.4%	11.2%	3.2%

In the case of ante-dating in the majority of instances the discrepancy was less than one week, and in no case did the period exceed 3 months.

Post-dating, on the other hand, was not very common but showed a wide range of variability, sometimes exceeding six months. In some instances the birth had been entered in the wrong *hatchitta* and reshuffling of entries had to be done to provide a complete list for such villages. A number of births were found in the registration lists which can only be assumed to be fictitious, as detailed inquiries in the village and from the chowkidars themselves failed to locate the births.

tions of illiterate recorders are only too obvious in the defective registration. Accurate registration is essential to economical health planning. Obviously the number of abortions, still births and maternal deaths elicited is too small to offer a reliable guide. Examination of the causes of death including as they do such a high proportion of 'not known' also offers little light, although it is clear that the infant deaths of known cause occurring within a week of birth could all have been associated with the uncontrolled mechanics of labour or indifferent technique on the part of the delivering agent or person cutting the cord. (By the local *daits* the cord is cut with bamboo fibre which, even if

sterilized by boiling, retains its capacity to sever the cord readily. Boiling is not resorted to, as a rule, and tetanus features as a cause of death in the deaths within a week, between a week and a month, and more doubtfully, between one and three months.) The other deaths of known cause within a month appear associated with poor prenatal condition of the mother or with indifferent infant hygiene.

Let us look then at the distribution of infant deaths at the various age periods. It is the high proportionate death rate within a month of birth (68 per cent) which offers clearly a clue to the major needs of the pregnant women and infants. Lack of prenatal care, absence of, or neglect to obtain, trained service at the time of delivery combined with poor hygiene service for the new-born infant are here clearly defined.

## II. Utilization of the data for planning

This information makes it possible to decide the main points of the programme.

1. It is evident that Tarakeshwar is the natural centre of the area of communications, and activities, social and medical and so must form the chief base for work.

2. *Medical aid to women and children* must be developed there, to include institutional care of pregnant women, of delivery and gynaecological cases and of infants and children. The best method of effecting this would be by appointment of a woman doctor, provision of 4 delivery and 2 prenatal beds, equipment and drugs and the establishment of a weekly prenatal and infant clinic at the hospital. Free transportation (based upon the hospital) from the villages to the hospital, for sick women and children is also required. Funds are not lacking to the religious endowment for this purpose.

3. *Clinical prenatal care by a qualified medical woman* (preferably the doctor suggested for charge of the women's beds and outdoor in the Tarakeshwar hospital) is essential to check physical and obstetrical abnormalities, with which the large early infant death rate is associated. This care must be supplemented by correctives for the major diet-deficiencies, i.e. by distribution of milk, germinated gram, yeast and iron.

Clinics should be arranged so that as far as possible the prenatals of each village can attend a clinic within  $1\frac{1}{2}$  miles of their homes at least once a fortnight and at the main centre once a week. This would mean a fortnightly prenatal and infant clinic in the villages (two each week) and a weekly clinic for prenatals and infants and one for sick children at the hospital in Tarakeshwar, the latter clinic as well as that at Loknath affording facilities for correction of abnormal health conditions and of obstetrical abnormalities. Suitable villages would be Chandpur (to serve Teghari, Chandpur, Santoshpur), Guria (to serve Guria, Bhata, Gaveshpur, Bistubati), Loknath (to serve Loknath, Bajitpur, Aligori and Baidyapur), Tarakeshwar (to serve Shapur,

Tarakeshwar, Bhimpur, Naupara), and Banjipur (to serve Howli, Bhananpur Dhalyan, Sainto). On the days when the woman medical officer takes the village clinics, i.e. two days a week, the treatment of emergency cases coming to hospital can be carried out by the male doctor in charge of the hospital.

4. *Training of the present local agents of delivery is called for.* In view of the findings, this will entail :—

(a) Intensive propaganda in the homes, not only among the women but also among the men folk, *through all possible channels*, (1) upon the need for technical help at delivery, the importance of rest and nursing for the women after delivery, the need for proper care of the new-born infant, (2) upon what a properly trained *dai* can do to help a woman during labour and after.

(b) Instruction and supervision of the practising *daïs*, instruction not only in elementary prenatal maxims and delivery service but in simple postnatal care and infant hygiene.

(c) Refresher courses in obstetrics and infant care for medical practitioners in the area, to provide, for all, sound medical maternity service in the area either upon payment by the family or through subsidy by the local authorities. This is probably best developed by a provincial policy.

5. *Establishment of early contact with the infant by the health staff* and instruction of the mother in infant care must also be an item of the programme. Because of the long distances to be covered, early contact must depend upon *notification of birth* to the health staff within a few hours of delivery by post card or messenger, by either the parent or the agent of delivery.

6. *Health protection of the older infant*, including vaccination at 5 months, by routine home and clinic contact if the other routines permit.

*Health staff required for the area :* (a) Woman doctor located in the hospital for clinic and maternity service, (b) supervisory midwife for *daïs* training and supervision of cases in the homes, (c) trained *dai*, (d) 1 health visitor for propaganda six months in the year, (e) 1 health assistant or child's help.

Salaries are not suggested as locally trained personnel should be recruited for posts (b), (c), and (e).

The thanks of the authors are due to Miss Balwant Kaur, Senior Health Visitor, to Miss Norah David, Health Visitor, the other members of the Health Staff of the Section, to Mr. Akkori Mukherjee, member of the Tarakeshwar Union Board, and to Mr. Taraknath Mukherjee, Chairman, District Board, Hooghly, for co-operation in the survey.

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## APPENDIX

Schedule for the collection of vital statistics to plan 'public health administration in maternity and child welfare in rural area

1-2. Union Board :	3-4. Village No.				5-7. Serial No.	
8. Result of pregnancy :	Abortion 1	Still birth 2	Live birth 3	Twins 4		
9. Maturity :	Premature 1	Full term 2				
10. Nature of delivery :	Normal 1	Forceps 2	Craniotomy 3	Podalic version 4	Caesarian section 5	
	Other operative procedure 6					
11. Classification of birth :	Resident 1	Non-resident 2				
12. Area of delivery :	In the village 1		Outside but within registration area 2	Outside 3		
13. Place of delivery :	Home 1	Hospital 2	Maternity centre 3			
14. Agent at delivery :	Doctor 1	Midwife Health visitor 2	Midwife 3	Dai 4	Relative 5	No one 6
15. Birth registration :	Yes 1	No 2				
16. Accuracy of date of birth registered :	Correct 1	-1 week 2	-1 month 3	-3 months 4		
	-6 months 5	Over 6 months 6	Ante-dated 7	Post-dated 8		
17. Longevity :	Alive 1	Dead 2	Contact lost 3	-1 week 4	-1 month 5	-3 months 6
	-6 months 7	-9 months 8	-1 year 9			
18. Place of death :	In the village 1		Outside but within registration area 2	Outside 3		
19. Death registration :	Yes 1	No 2				
20. Age at death as registered :	-1 week 1	-1 month 2	-3 months 3	-6 months 4	-9 months 5	
		-1 year 6	+1 year 7			
21. Cause of death :	Dystocia 1	Prematurity 2	Tetanus 3	Congenital debility 4		
	Septicæmic 5	Diarrhœa 6	Marasmus 7	Fever 8	Pneumonia 9	
	Infectious fever (specify) 10		Other (specify) 11	Not known 12		
22. Maternal life :	Died within a month 1	Died within 3 months 2	Alive after 3 months 3			
23. Place of death :	In the village 1		Outside but within the registration area 2	Outside 3		
24. Death registration :	Yes 1	No 2				
25. Age at death as registered :	-1 month 1	-3 months 2	Over 3 months 3			

*Hint in filling up the schedules.*—Circle a number only if information is available. For example, if the nature of delivery is not known, do not circle any of the numbers in column 10. If a normal delivery, circle 1 in column 10. If the birth is registered but post-dated by 20 days circle 3 and 8 in column 16.

## Current Topics

### Intramuscular Injection of Mepacrine (Atebrin): Histological Effect

By F. HAWKING, D.M.

(Abstracted from the *British Medical Journal*, ii,  
14th August, 1943, p. 198)

A REVIEW of the literature shows that intramuscular injection of mepacrine (atebrin) is considered to be free from local reaction in most cases, to cause pain and swelling in some cases, and to cause local abscesses in rare cases.

Mepacrine methanesulphonate (atebrin musonate) was injected intramuscularly and subcutaneously into rabbits and rats. The macroscopic lesions were often inconspicuous, but microscopical examination always showed a certain amount of necrosis at the site of injection. The damage caused by a therapeutic injection of mepacrine is similar in kind to that caused by a therapeutic injection of quinine, but probably less than one-third as extensive. For patients who cannot take mepacrine by mouth this local damage does not contra-indicate parenteral injection, but its occurrence should be borne in mind when choosing between the intramuscular and the intravenous routes.

### Tanret Reaction in Subtertian Malaria

By J. W. HOWIE, M.D.

MAJOR, R.A.M.C.

and

R. M. MURRAY-LYON, M.D., F.R.C.P.L.

MAJOR, R.A.M.C.

(Abstracted from the *Lancet*, ii, 11th September, 1943,  
p. 317)

TANRET tests for quinine were done on all urines of 100 British soldiers admitted to hospital suffering from subtertian malaria in Southern Nigeria and on 53 men in normal health.

Reactions were examined during acute attacks treated by gr. 30 of quinine by mouth daily for 7 days, and during convalescence after the daily suppressive dose of gr. 5. Precautions were taken to ensure that the drug was swallowed.

Of the 100 patients, 88 who showed positive reactions in every urine during treatment of the acute attack made rapid recoveries.

After gr. 5, all the 53 normal men showed positive reactions, but these did not appear within 15 minutes and persist for 24 hours as they are commonly supposed to do. Only 20 men showed positive reactions within an hour, the others became positive between 1 and 5 hours.

By comparison with these standards some deficiency of quinine excretion was shown by 24 of the 100 men; 6 were deficient only in the acute attack, 12 only in convalescence and 6 in both acute attack and during convalescence.

In 7 men quinine was absent from all urines during the acute attack. They remained seriously ill until given intravenous quinine; then they showed positive

Tanret reactions in all urines and recovered rapidly. Only one had negative reactions in convalescence.

A group of 5 men who showed positive reactions at irregular intervals during the acute attack recovered slowly and showed negative reactions during convalescence.

The 6 men whose excretion was deficient both in the acute attack and during convalescence had all suffered repeated attacks at short intervals.

The findings are discussed and their relation is considered to the condition of 'continuous infection', which commonly precedes blackwater fever. The need for adjusting quinine courses in individual cases, in relation to quinine metabolism is emphasized.

### CONCLUSIONS

Despite precautions to ensure that quinine was being regularly taken, 24 out of 100 malaria patients showed negative Tanret reactions in all or many of their urines during treatment and convalescence.

Their responses to quinine treatment compared unfavourably with those whose Tanret reactions were regularly positive.

It is suggested that quinine administration and dosage in treatment and daily suppression (prophylaxis) should be controlled and adjusted for each individual by using the simple Tanret test in the way described.

### Tannic Acid and Liver Necrosis

(From the *Lancet*, ii, 21st August, 1943, p. 229)

THE treatment of burns by the local application of solutions of tannic acid, introduced by Davidson in 1925, was quickly hailed as a great advance, so that before long most burns were dealt with by immediate tanning. In time various minor modifications of the original method were adopted by different surgeons—slow and rapid tanning, and the combination or succession of solutions of tannic acid and silver nitrate. The death rate from burns, in almost all the published figures, rapidly fell from 1925, and although part of this improvement must be attributed to concurrent advances in the treatment of shock and dehydration, much of it seemed clearly to be due to the tannic-acid treatment. When this war began, burns were quickly recognized to be a greater hazard than in all previous campaigns, and tannic acid was at first almost universally employed. Doubts soon began to arise about the tanning of burns of the face and hands, because of late contracture, but this point need not concern us here. Severe burns still too often ended fatally in spite of treatment, and active investigations into the many problems involved—shock, dehydration, toxæmia, acute duodenal ulcer and so on—were being pursued before the war, especially by Wilson and his colleagues in Scotland and later in the Middle East. In 1938 they had reported severe necrotic damage to the liver in fatal burns, and Belt described the hepatic changes in detail. Wilson's observations aroused suspicion of the toxicity of tannic acid, as he was able to demonstrate a similar liver lesion in animals injected with tannic acid or sodium tannate. His subsequent work is mainly contained in confidential service reports, but last year Wells, Humphrey and Coll in America described severe liver necrosis in fatal human burns, and reproduced this lesion in rats by injecting tannic acid. As Barnes and Rossiter point out, it seems that the special type of liver damage (universal central necrosis of lobules) was not seen before tannic acid was used in treatment, and Allen and Koch who have not used the tanning method found no liver damage in any of their fatal cases. The observations of Wells and his colleagues, as they became widely known, rapidly began to shake confidence in tannic acid, and many surgeons turned to other methods, new or old. Lately, for example, Pendleton has drawn attention to the advantages of a spray of paraffin wax, sulphanilamide and other

ingredients, an adaptation of the 'Ambrine' popular in the last war. Erb, Morgan and Farmer have published an account of 61 fatal burns, all examined carefully by the same pathologist (Erb) between 1920 and 1942. In all, 41 of the cases had been tanned, and 25 of these showed definite hepatic necrosis at autopsy, while this lesion was completely absent in 21 untanned patients. Their records seem to bear out the great reduction in the mortality of burns after tannic acid was first used in 1925—from 32.2 per cent to 11.8 per cent—but they add that the introduction of sulphonamides and other methods have further reduced the mortality. A fact also brought out by their figures is the transfer, after tannic-acid treatment, of the main mortality from the primary period of shock (12-36 hours) to the period of toxæmia (3-6 days), the time when the necrotic lesion in the liver is most often found.

As these facts accumulated, it became clear that the toxicity of tannic acid, its relation to the hepatic damage noted, and the question whether this method of treating burns should be abandoned all required active investigation, and much work has been done on these lines both here and in America. Cameron, Milton and Allen, whose paper appeared in these columns last week, have experimentally investigated the toxicity of tannic acid when introduced into the animal body by various routes, and the chances of its absorption through burnt surfaces. They show that gallic acid, often contained in commercial samples of tannic acid, is harmless, but prove conclusively that tannic acid is a toxic drug. Its main effects are hæmorrhage, great œdema at the site of injection, loss of plasma proteins, renal damage and hepatic necrosis. The main part of the liver lesion is a coagulation necrosis of the centres of all the lobules. In the later stages of non-fatal experiments they note the early evidence of the remarkable power of the liver lobules for repair. Their experiments leave no doubt that tannic acid is absorbed from large burnt surfaces, and can be demonstrated in the tissues, including liver and kidneys, by suitable tests. Barnes and Rossiter describe in this issue how to obtain burned surfaces of more or less uniform size for animal experiment. They confirm in general all the toxic effects of parenteral administration, and report slight liver damage after the application of tannic acid to a fresh burnt area, amounting to about a quarter of the body surface of a guinea-pig. They lay stress on two other effects of tannic-acid applications, not previously noted—a higher mortality in the tanned animals, and a striking loss of weight as compared with controls. With Clark, Rossiter has demonstrated impaired liver function in rabbits injected with tannic acid, the results being more variable after intravenous than after subcutaneous injection, presumably because the toxic effect is more sustained with the latter route. These workers are rightly cautious in interpreting their experimental results. Cameron and his colleagues claim only to have proved the toxicity of tannic acid in animals, and that the drug can be absorbed through raw burned surfaces; the Oxford workers confirm this.

In the end the tannic-acid treatment of burns must stand or fall on the clinical evidence, and the records of Erb, Morgan and Farmer of Toronto already show that great caution is required in tanning large burnt surfaces. There is clearly a great difference between the effects of tannic-acid injection and its application to a burn, and even if slight hepatic damage, rapidly capable of repair, occasionally ensued from tanning a small or moderate sized area, this would not condemn the method provided it had advantages over all the others available. It has lately been claimed, however, that disadvantages, such as slowness of healing under the dense and firm tan, outweigh the advantages of the method. It seems possible that newer procedures, now under trial, will entirely supersede tannic acid, or that tannic acid will remain the application of choice for smaller burns of the body requiring immediate treatment in difficult circumstances such as on the battlefield or at sea.

## Some of the Things the General Practitioner should know about the Electrocardiogram

By J. M. BAMBER

(Abstracted in the *International Medical Digest*, Vol. XLIII, August 1943, p. 77)

THE electrocardiogram is of great value in the diagnosis of heart disease but there are many mistakes made in the interpretation of the curves. 'People are made unhappy and their activities restricted unnecessarily by the lack of knowledge of just what the electrocardiogram means to the individual patient.

'Every person who has heart disease does not need an electrocardiogram, but no patient can be said to have had a thorough examination unless an electrocardiogram is made. People with large hearts, with congestive failure caused by old rheumatic valvular disease or hypertension, or cases of luetic heart disease with wide-open aortic regurgitation with congestive failure, do not need electrocardiograms unless there is irregularity of the heart that is not understood from the clinical examination.

'It must be remembered that a normal electrocardiogram does not eliminate the possibility of heart disease. Cases of angina pectoris are frequently seen in which the electrocardiogram is normal, and normal curves have been noted a few hours before coronary occlusion and even when the patient was in pain. Furthermore, the electrocardiogram is of little help in prognosis. It should be considered only as a part of the examination, and balanced with the history, physical findings and in some cases, x-ray, blood count, and so on.

'It is a mistake to accept minor changes in the electrocardiogram as proof of heart disease and so inform the patient, thereby running the risk of starting a neurosis that may take months or years to overcome. Patients are sometimes told that they have heart disease, when the opinion is based on an electrocardiogram that, according to . . . present standards, is within normal variations. Such an error may play havoc with the peace of mind of both the individual and his family.

'There is a tendency on the part of some practitioners to depend too much on the electrocardiogram and to neglect the clinical picture. The training of one who reads the curves is of vital importance.

'Occasionally curves are seen that are definitely abnormal, especially in the electrocardiograms of people in middle or later life. These abnormalities are caused by some small lesion in the conducting system. They are too small to affect the function of the heart, and since they are not progressive, do not affect the well-being of the individual. Puzzled by some vague symptom, if the physician grasps this as proof of clinical heart disease and passes this diagnosis on to his patient with restrictions and treatment, he may do more harm than good. Persons in this group should be classed as subclinical and need no treatment other than sensible living and moderation in all things. 'Some will develop clinical heart disease and die; others will develop clinical heart disease and live out their lives; still others will live into old age without showing any clinical signs of heart disease, the electrocardiogram remaining constantly abnormal. The prognosis in these cases will depend on the clinical picture.

'Those who read electrocardiograms should determine whether the patient has taken digitalis or quinidine in the near past. More than three weeks are required in some cases, for the effect of digitalis to disappear. The physician should know whether the patient has smoked just before the making of the curve. The position of the patient, whether sitting or lying down, should be noted.

The writer presents several illustrative cases as a warning against some of the pitfalls in the use of the electrocardiogram.

'A 59-year-old farmer with no cardiac symptoms was examined in March 1941. A complete physical examination was negative, although the electrocardio-



gram was definitely abnormal. The T waves were inverted in all chest leads; flat in lead I; upright in leads II and III. If this man had presented symptoms that could have been considered as due to heart disease and his physician had ordered an electrocardiogram, the curve would have shown definite evidence of myocardial disease and the patient would probably have been restricted in his activities unnecessarily. In the absence of physical findings, no treatment or restrictions were advised and at the end of two years he still remains well and at work. This case brings out the fact that persons in middle life can present definitely abnormal electrocardiograms, and go happily on their way without symptoms.

The error is sometimes made by depending on one electrocardiogram, as in the following instance. A 56-year-old man was seen in February 1939, complaining of having suffered in the previous three days three attacks of severe pain across the front of the chest and radiating into each arm. The attacks developed while the patient was at rest and one attack lasted nearly three hours. He was examined about 12 hours after the last attack. The man felt a little weak, but otherwise made no complaint, had no fever and no leukocytosis. The findings of the physical examination were essentially negative and the electrocardiogram was entirely normal. The patient continued to feel well, but four days later the electrocardiogram was definitely abnormal. It was not typical of myocardial infarction but showed that something had happened to the myocardium. A diagnosis of myocardial infarct was made. The patient rested for a month and then returned to his work, having had no more cardiac symptoms. He died two years later from other causes. Autopsy showed that he had had a small infarct. There might easily have been some question about the diagnosis in this case if only one electrocardiogram had been made.

'If the patient has an abnormal electrocardiogram and has atypical symptoms, one should be careful not to consider the symptoms due to clinical heart disease merely because the electrocardiogram happens to be abnormal.' In 1928, the writer examined a 61-year-old woman who suffered precordial pain but gave a rather vague description of pain which was not associated with exercise. She also complained of shortness of breath and swelling of the lower extremities. The electrocardiogram showed complete left bundle-branch block. The clinical picture here presented might well lead to diagnosis of heart disease with congestive failure. The electrocardiogram was certainly abnormal, but the physical examination was essentially negative. On careful study it was found that the shortness of breath of which she complained, was sighing respiration. The swelling of the lower extremities was found to be due to varicose veins. The chest pains were not typical of angina; there was no valvular disease and the blood pressure was normal. There was no history of hypertension and the heart was normal in size. The electrocardiogram was the only real evidence of heart disease. After 15 years she is working part time. She has a few of her old symptoms but complains much less than when first seen. The electrocardiogram still shows bundle-branch block. She recently walked 70 city blocks without distress.

'One can see that this patient's symptoms might have been misinterpreted and the electrocardiogram could have been used as positive proof of serious myocardial disease. She evidently had some disease of the myocardium involving the conducting system, but it was not progressive and it has caused her little trouble in the last 15 years. This case is mentioned to show that even in the presence of an abnormal electrocardiogram, symptoms are not necessarily due to heart disease unless they are typical. In other words, the changes in the myocardium may be so slight that they do not disturb the function of the heart even though they change the electrocardiogram.'

'On another occasion a man 61 years' old was examined whose findings were essentially negative, except that he was over-weight. The electrocardiogram was exactly like that of the woman just mentioned,

but the man presented a typical angina of effort. He lived only a little over four years from the time he was first seen, and died from heart disease. The electrocardiogram in these two cases looked just alike; each was definitely abnormal. The clinical picture was the differentiating factor.

'To give another instance of the prime necessity for the correlation of clinical findings with the electrocardiogram in making the diagnosis, the following case is cited.' In 1936 the writer examined a 22-year-old male office worker. He was large, well-developed and healthy looking, but gave a history of attacks of fast beating of the heart. He had been examined by several doctors and no signs of heart disease had been found. The electrocardiogram showed a peculiar type of curve: short PR interval—wide QRS complexes. This type of electrocardiogram is typical of what is known as the Wolf-Parkinson and White syndrome, and is generally considered not to be evidence of heart disease, most of these patients suffering from attacks of paroxysmal tachycardia. Following this original electrocardiogram, the report had gone back to the physician that the electrocardiogram showed myocardial disease. The patient and his family had been advised accordingly and a great deal of alarm and distress had been created as to the patient's future. On examination, this young man showed no evidence of heart disease. The electrocardiogram was at times abnormal, at times normal. Anyone who reads electrocardiograms should know of this condition, as a great deal of harm can be done when a mistaken diagnosis of serious heart disease is made. The young man is now an officer in the U. S. Navy.

'This case brings out the fact that it is unwise to make a diagnosis of disease of the heart in the young, when no significant physical findings are discovered in a thorough examination. In rare cases this is not true, notably in rheumatic fever and acute infections, such as diphtheria. Under these circumstances, the changes in the electrocardiogram may be the only evidence of cardiac involvement.'

'When a physician sends a young patient for an electrocardiogram, and he receives a report that the electrocardiogram shows definite evidence of myocardial disease, he should review the case thoroughly. When there is no enlargement of the heart and no significant murmur can be heard, he should be slow in making a diagnosis of organic disease. There are exceptions, however, as in the case of small children.'

'An 8-year-old girl was examined some time ago whose complaints were irritability, poor appetite, failure to gain weight and an occasional rise in temperature above the normal. There were no joint symptoms. Physical examination was negative except for a faint systolic murmur heard in the apex. This kind of murmur is frequently heard when the heart is sound, but the electrocardiogram in this girl showed the first stages of A-V block with wide and slurred QRS complexes, and thus a diagnosis of active rheumatic fever was made.'

The physician sees a number of patients supposedly having heart disease who really have perfectly sound hearts. 'People with neurocirculatory asthenia, with palpitation, dyspnea, chest pains, or some insignificant murmur, make up a large percentage of the mistaken diagnosis. . . . If these patients are sent for an electrocardiogram and too much is read into it, this report going to the physician or patient makes a bad matter worse.' Patients present themselves for examination who, in the writer's opinion, have no heart disease. They come bringing with them one or more electrocardiograms with reports written in plain English of 'evidence of myocardial disease'. 'It is a grave mistake for doctors to put reports of this kind into the hands of patients. One can see how serious this would be in the case of some nervous individual who has no heart disease, even though the report might indicate that he has. As a rule people are more frightened by a diagnosis of heart disease than any other ailment. In a few weeks' course on electrocardiography, it is impossible to learn enough to be competent to make



proper evaluations. Time and study are required for this.

The electrocardiogram is of great aid when properly evaluated, and in any case, where the status of the heart is in question, the patient should be given the benefit of it, but with a clear understanding that it is only a part of the examination.

### Virus Pneumonias

(From 'The New York State Journal of Medicine,' Vol. XLIII, 1st January, 1943, p. 26)

THE problem of pneumonias due to bacterial agents, although not completely solved, has nevertheless been gratifyingly modified in the majority of pneumonia patients. The causative organism can usually be demonstrated in the sputum or from nasopharyngeal cultures; the clinical and x-ray pictures have been well defined, and a definite regimen of treatment by chemotherapy and other measures has been standardized. The improvement in the prognosis of bacterial pneumonias has been one of the most satisfying features of modern medicine.

A familiar pneumonic syndrome, strikingly different from the above, has been reported in the literature with increasing frequency.<sup>1,2,3,4</sup> The following are some details in which this 'atypical' pneumonia differs from the ordinary or classic pneumonia:

The incubation period may be longer, sometimes as long as two weeks. The cough is unproductive and apt to assume a hacking nature. The temperature curve is more regular, rises slowly, and falls by lysis in from a few days to two to three weeks. Headache, photophobia, and sweating are frequent concomitant symptoms. The leukocyte count is essentially normal. No bacteria found in the sputum or rhinopharynx can be associated with the disease. The pneumonic signs and x-ray picture are those of scattered infiltrations, often of a migratory nature. Sulphonamide therapy is futile; complications are unusual; and the mortality is low. In the few autopsies reported, the histologic reaction of the involved lung has been composed chiefly of mononuclear cells, and no bacteria have been found.<sup>5</sup> Cytoplasmic inclusion bodies have been observed in the lungs of infants dying of this form of pneumonia.<sup>6</sup> Because of the atypical clinical and x-ray findings, the pathologic reports of a mononuclear reaction in the areas of pneumonitis, and the resemblance of this response to the pneumonias caused by known virus agents, the term 'virus pneumonia' has been suggested for this peculiar but definite pneumonic syndrome.<sup>7</sup>

Attempts to find the direct causative agent in such pneumonias have led to the isolation of a virus which differs from the previously known influenza virus.<sup>8</sup> Further research into the virus that causes this form of pneumonitis, by means of immunologic studies and neutralizing tests, has brought to light a remarkable cross relationship between this pneumonic virus, or viruses, and those of psittacosis, meningopneumonitis, and lymphogranuloma venereum.<sup>9</sup> This opens a fascinating field in the study of pneumonias and their relationship to contagion to and from animals, including household pets.

Suffice it to say that it is of the utmost importance to be able to recognize or suspect this pneumonic syndrome and its epidemiologic implications. A simple, confirmatory test may be the demonstration of inclusion bodies in the large mononuclear cells in the stained sputum of patients who have this disease.<sup>10</sup> One of the sulpha drugs may be employed, with the thought of preventing secondary invasions, which are not uncommon in influenza pneumonia.<sup>11</sup> If a short period of observation reveals no effect from the drug, it is wise to discontinue its use; otherwise toxic effects may ensue, to the detriment of the patient's condition.

<sup>1</sup> BOWEN, A. (1935) .. *Am. J. Roentgenol.*, **34**, 163-174 (Aug.)

<sup>2</sup> ALLEN, W. H. (1936) .. *Ann. Int. Med.*, **10**, 441-446 (Oct.)

- <sup>3</sup> REIMAN, H. A. (1938). *J. A. M. A.*, **111**, 2377 (Dec. 24).  
 REIMAN, H. A., and HAVENS, W. P. (1940). *Arch. Int. Med.*, **65**, 138 (Jan.).  
*Ibid.*, (1942). *Ibid.*, **70**, 513 (Oct.).  
<sup>4</sup> LONGCOPE, W. T. (1940). *Bull. Johns Hopkins Hosp.*, **67**, 268 (Oct.).  
<sup>5</sup> ADAMS, J. M., GREEN, R. G., EVANS, C. A., and BEACH, N. (1942). *J. Pediat.*, **20**, 405 (April).  
<sup>6</sup> FRANCIS, T., Jr., and MAGILL, T. P. (1938). *J. Exper. Med.*, **68**, 147 (Aug.).  
<sup>7</sup> RAKE, G., EATON, M. D., and SHAFER, M. F. (1941). *Proc. Soc. Exper. Biol. and Med.*, **48**, 528 (Nov.).  
<sup>8</sup> FINLAND, M., PETTERSON, M. D., and STRAUSS, E. (1942). *Arch. Int. Med.*, **70**, 183 (Aug.).

### Individual Specificity of Human Serum

(From the *Lancet*, i, 19th June, 1943, p. 784)

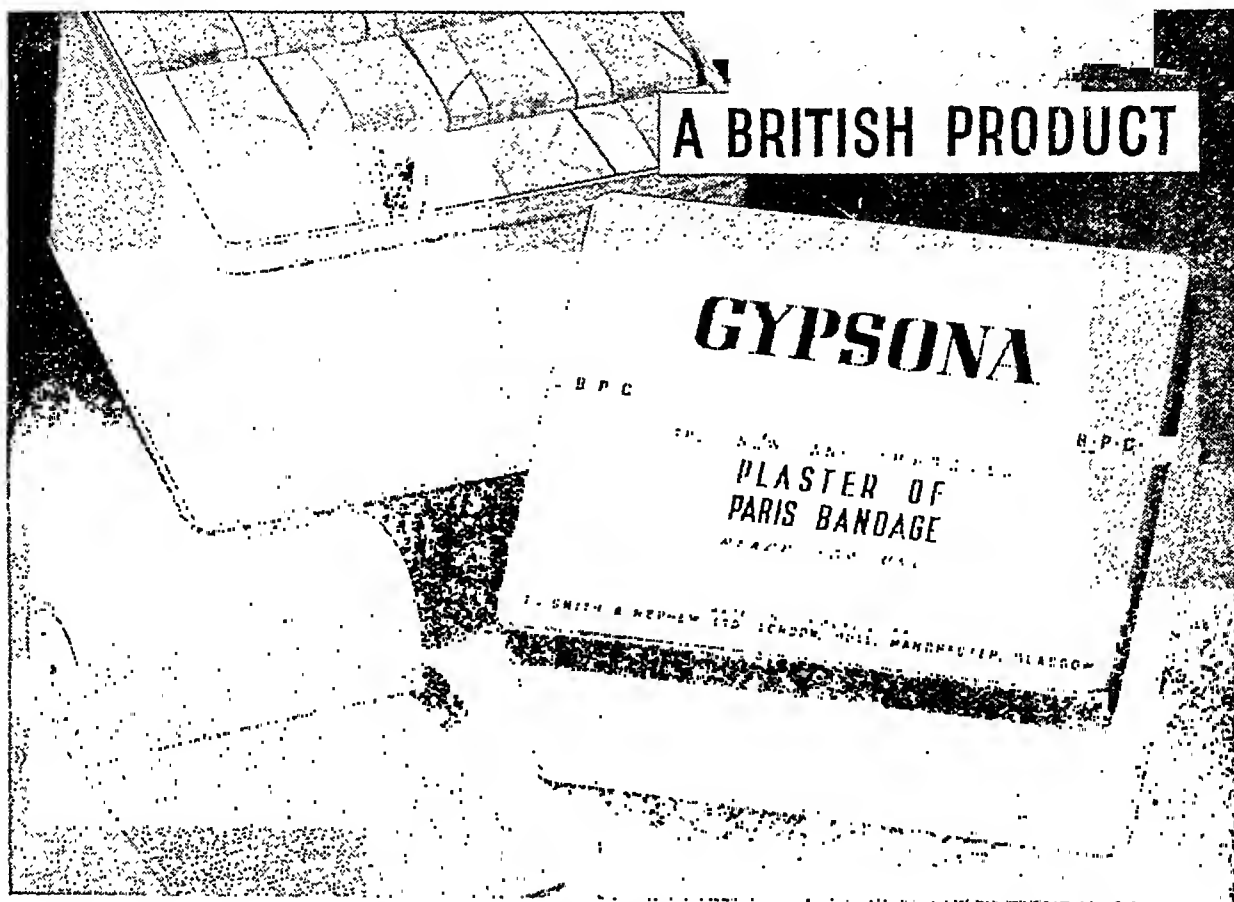
REACTIONS after blood transfusion may be divided into hæmolytic and non-hæmolytic. The latter may be due to some component of the plasma of the donor or to extraneous matter. The importance of contamination of the sodium citrate solution, or of the apparatus used, has been repeatedly stressed by American authors as a cause of febrile reactions and it has been pointed out that as the standard of care in the preparation of apparatus increases, so does the incidence of transfusion reactions diminish. Nevertheless, the view that all non-hæmolytic transfusion reactions are due to the introduction of extraneous matter seems untenable. Some recipients seem peculiarly liable to develop reactions, even when the greatest care has been taken in the preparation of the transfusion fluid. Recent experience with plasma and serum transfusions has suggested that human plasma may contain antigenic substances which may react with corresponding antibodies in the recipient's serum. Only recently however have such antigens actually been demonstrated in human sera. Cumley and Irwin proceeded in much the same way as did Landsteiner and Levine in the demonstration of the M and N factors in human erythrocytes—that is to say, by injecting human material into animals and then testing the immune animal antisera against a number of samples of human material. Injections of human serum were administered intravenously to rabbits. Later, the rabbit was bled and ring tests were carried out with the serum obtained against a number of samples of human sera. No difference was obtained by direct testing but when the rabbit serum was first absorbed with a given human serum it would still react with other human sera. Using this technique at least 3 'groups' of human serum could be recognized and these were not in any way related to the Landsteiner ABO blood groups. These serum differences are probably constitutional and if so, their importance from the genetical point of view will be considerable. In any case the possible bearing on the aetiology of certain transfusion reactions opens up yet one more field of research in this rapidly growing subject. It is not too fanciful to foresee a time when in addition to carrying out compatibility tests in relation to the red-cell agglutinogens, transfusions will be preceded at least in certain cases by a ring test between the donor's and recipient's plasma.

### Transplantation of the Ureters into the Large Bowel

By G. G. TURNER

(From the *British Medical Journal*, ii, 30th October, 1943, p. 535)

THIS subject has always interested me, for at the outset of my surgical career I saw cases of ectopia which made me realize the utter misery of the sufferers, so often to become unwanted outcasts who, like Job,



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survived to 'curse the day wherein they were born'. Treatment was most unsatisfactory, and though transplantation of the ureters into the bowel seemed the best solution I was brought up in the belief that the operation was extremely dangerous and sure to be followed by ascending renal infection and rapid death; the only justification for a return to the subject is because some members of the profession still appear to be obsessed by this fear.

For me the bright lamp of surgical progress in this field was lighted in 1911 when Stiles of Edinburgh read a paper in Denver City on two cases in which he had successfully transplanted the ureters by burying them obliquely in the wall of the bowel, in much the same way that the catheter is buried in the stomach wall in the Witzel method of gastrostomy.

#### AFTER-RESULTS

In 1927 I delivered a Hunterian Lecture on this subject, and was able to give the after-history of 17 personal cases from a few months to 15 years after transplantation (Turner, 1929). The subsequent history of these same patients after the lapse of a further

fellows. No. 1 has never been a big strong person, but he has developed quite well, played games, including football, and has always been ready for work when it was available. No. 2 is a brave woman now 51 years of age. Her first child was born three years after the operation, and both pregnancy and delivery were without unusual incident. Ever since the operation she has had some pain in the back, but it has only been very troublesome at infrequent intervals during the last five years. In 1938 a phosphatic calculus was removed from the right kidney, which was considerably dilated, and early this year a large calculus was removed from the corresponding ureter. The patient is now very well. Except for these attacks her health has been good, and her greatest happiness has been to look after her family and household. She has carried out all the domestic duties which fall to the lot of a North country woman of the artisan class. After her day's work she has often visited the pictures and has gone from home on holiday each year. For years no. 3 did the hard work of a general farm labourer. His marriage about three years ago was for companion-

*After-history of 9 cases of transplantation for congenital defects with incontinence. All previously reported (Turner, 1929)*

Case number	Sex	Age at operation (years)	Number in B.J.S., Vol. 17	Time since operation (years)	Present condition	Further particulars
1	Male	8	1	30	In good health.	Working long hours at munitions.
2	Female	22	2	29	"	Three children born since operation. Does all own household duties. Twice had stone removed from right kidney and ureter.
3	Male	19	3	25	"	Has worked as a farm labourer. Married.
4	Female	6	5	25	"	Stone removed from kidney. Married; no children.
5	Male	5	7	23	"	During one recent year several attacks of renal pain. Married.
6	Male	10	12	19	"	Trouble with inguinal hernia. Otherwise well. Does heavy work.
7	Male	8½	15	17	"	Nephrectomy for pyonephrosis—persistent urinary fistula. Does heavy work down a mine.
8	Male	3	16	16	"	
9	Female	3½	17	16	"	Has always been splendidly well.

16 years is now presented (see Table). The numbers of the cases recorded in the original paper are placed in the fourth column. The patients have been very closely watched, and those who have been admitted to hospital for various reasons have been submitted to detailed examination. In no case has there been gross evidence of renal deterioration. In 1936 J. H. Saint examined several of these patients by the method of intravenous pyelography, and the results were published in a joint paper (Turner and Saint, 1936). In the original 17 cases there were four deaths directly due to the operation (peritonitis 3, septic dermatitis 1). Three patients subsequently died—from intestinal obstruction, sepsis following a plastic operation after removal of the ectopic bladder, and hæmorrhage after plastic repair of the penis respectively. Thus none of the patients who recovered have subsequently died because their ureters were transplanted. Of the 9 surviving cases the essential details are set out in the accompanying table.

In case 7 an enormously dilated ureter could not be buried and was simply tucked into the bowel end to the side. In case 9 a submucous bed was prepared. In the other cases the original method of Stiles was used, one ureter being implanted at a time and with a varying interval between interventions. Full details of the operations are given in the original paper. 'In good health' means that the patients can stand up to their environment and take their place among their

ship, but is not entirely Platonic. Case 4 has also had a stone removed from the right kidney 14 years after the transplantation; but she has always been well and active, carrying on the work of a ladies' hairdresser, which in her case entailed a considerable amount of travelling. Three years ago she married, and is anxiously awaiting maternity. No. 5 was a feeble child but has developed into a sturdy young fellow. Four years ago he was exceptionally well, was working long hours, and dancing in the evenings by way of relaxation. During the past twelve months he has had several attacks of renal pain; but these symptoms left him after passage of a considerable amount of grit, and he is now working regularly in charge of a factory. No. 6 has enjoyed good health except for troubles due to double inguinal hernia, one of which had to be operated upon in a state of strangulation; but despite this handicap he puts in a long day as a craneman. No. 7 has had a tedious time with many vicissitudes, including nephrectomy for pyonephrosis. None the less he is well developed, strong and active, and capable of hard work. No. 8 has been difficult to keep in touch with, but he is reported to be well and strong. No. 9 was operated upon at an early age, but she made an easy recovery, has developed normally, has never shown any untoward symptoms, and has grown into an attractive girl who enjoys excellent health. Many other cases operated upon since the above series have been equally satisfactory, and I would just recall a charming girlie

born with an ectopic bladder whose parents were thrown into the depths of despair as the result of the utterly pessimistic outlook of the consulting surgeon who was called to see the case a few days after birth. The transplantations were carried out between 3 and 4, and now, eight years later, the child is perfectly well, highly intelligent, and especially fond of swimming. Also another girl, who wrote four years after operation: 'I have to catch a bus in the mornings at a quarter to eight in the black-out, but it is fun!' An officer whose ureters were transplanted just previous to total cystectomy for neoplasm is now, two years later, back to his military duties, albeit on the home front, while in like case a street trader is actively employed in his traffic. I used to feel that every case of transplantation would sooner or later show some evidence of ascending infection, but I am now hopeful that with the great simplification of the technique there may be many in which it never occurs. The exact condition of these patients may be regarded as the results of an experiment in applied physiology, and can be detailed as follows.

#### DETAILS OF RESULTS

*Effect on the economy of the body.*—Just after the transplantation the patients are invariably abnormally thirsty, and this may continue for about a year. During this period they often lose weight, and sometimes very considerably. After this time thirst diminishes and they not only regain lost weight but begin to put on flesh, so that they come to look plump and well nourished. Appetite is usually good and mental acuity more than average. They behave like normal individuals, are cheerful and happy, and able to work and play like others of their station. They can also stand up to the buffets of their environment, including physiological processes like pregnancy, operations, and illness.

*Rectal function and control.*—In nearly all my cases this has been satisfactory, though in two of them continence during the night has never been acquired, though these same patients have complete control by day. While there is some variation, most patients can hold the contents of the rectum for three or four hours at a stretch, and the call is not so urgent but what they can await a convenient opportunity with confidence. Some patients sleep throughout the night without being disturbed, while others may rise once or twice. All agree that the behaviour of the rectum is much influenced by the general health. With exhaustion or indisposition rectal calls are more frequent. The contents voided are usually an intimate mixture of faeces and urine, but sometimes the same patient may pass clear or opalescent urine at one time and a solid evacuation at another. The rectal mucous membrane is unaffected and, except for unusual moisture, looks normal when inspected through the sigmoidoscope.

*Where the urine is stored.*—At the time of my first communication many considerations led me to conclude that the urine was stored in the large bowel and not in the rectum. This conclusion is amply supported by urography.

*Effect on the kidneys and ureters.*—The changes in structure are sometimes very striking. In the first few weeks the ureters and pelvis may be dilated, and this dilatation may persist and increase. In the series of examinations made in collaboration with J. H. Saint four out of six patients showed a moderate degree of unilateral hydronephrosis, and in another the condition was bilateral. The most striking feature was the general good health of the patients examined. Marked unilateral hydronephrosis was also found in a patient who died subsequent to operation for intestinal obstruction, but that boy had enjoyed good health until his fatal illness. In nearly all of the earlier cases there was clinical evidence of some ascending renal infection, but for the most part it was transient and did not materially interfere with recovery. From the clinical aspect only those cases in which there has been obstruction in the lower ureter have suffered seriously. This is in keeping with general pathology, and conforms to the rule that infection with good

drainage is often neither very troublesome nor dangerous. The ureter may be dilated or may look normal, but the actual junction with the bowel and the opening into the lumen is not always demonstrable either by radiographs or by sigmoidoscopic examination. When visible it may take the form of a nipple with a terminal or lateral orifice, a rosette, or a tiny opening hidden behind one of the rectal folds.

#### SHOULD BOTH URETERS BE TRANSPLANTED AT THE SAME SITTING?

Up till quite recently I have always taken the view that it is safer to transplant one ureter at a time, and the wisdom of this course has been borne out by statistics. With better understanding of the problems involved, a simpler technique, and more knowledge of after-care, I am tending more and more to carry out a simultaneous transplantation, except in children, and even in them the hazards of a second anaesthetic may perhaps balance the only slight extra risk of the double transplantation.

#### WHAT IS THE BEST TECHNIQUE?

The technique has now been very much simplified, and is carried out without any special apparatus. Clamps are not used either for the ureter or for the colon. Coffey's tubes are no longer employed, and Charles Mayo's catgut guide has been discarded. The main points are to make an oblique implantation into a submucous bed in the bowel without kinking or compression and with due regard for the blood supply of the ureter. Compression from too tight suturing or the result of hematoma or traumatic oedema is probably the most harmful thing that can occur. Fine 3/0 or 6/0 chromic catgut is used throughout. Drainage is not employed.

#### PREPARATION AND OPERATION

Preparation will differ a little, depending on whether the surgeon is dealing with a congenital defect in an otherwise healthy child or the operation is for the relief of some condition, such as malignant disease of the bladder, likely to be associated with sepsis or general deterioration. No operation should be done until the renal function has been raised to as nearly the normal standard as possible. The bowel should be well cleared by a reliable purgative or by an enema not later than 12 hours before operation. If there is distension or constipation a full dose of castor oil is the best preparation. No attempt should be made to sterilize the bowel or even to cleanse it by repeated irrigation, which may result in the surgeon encountering a wet puddle in the pelvic colon. The choice of anaesthetic will depend partly on the condition of the patient and partly on the practice of the surgeon, but whatever method is employed complete relaxation is necessary. The patient is placed in the Trendelenburg position and the abdomen opened by one of the vertical incisions, which must be long enough to give ready access to the pelvis. I have made it a practice to transplant the right ureter first, but I am not able to give any valid reason for the choice. If both are to be transplanted at the same sitting I am sure that it should be into the same side of the bowel, and the right or inner side is the more convenient. To bring this about it is usually best to pick up the left ureter on the outer side of the sigmoid and to bring it through the mesocolon to the inner side, where it is made to enter the bowel about 1½ in. higher than its fellow. It is usually easy to identify the ureter as it crosses the pelvic brim. Spontaneous vermiculation, or this movement elicited by mechanical stimulation, is characteristic. The posterior peritoneum is incised in the length of the ureter for about 3 in., and the ureter is gently lifted from its bed and traced towards the bladder. Not more than 2½ to 3 in. should be isolated: in this respect illustrations in surgical journals are misleading. At the lower end the ureter is clamped and divided obliquely; the end is securely tied, and its open end carbolized and allowed to retract. The upper end is held by a suture passed from its lumen and out through its upper surface a quarter of an

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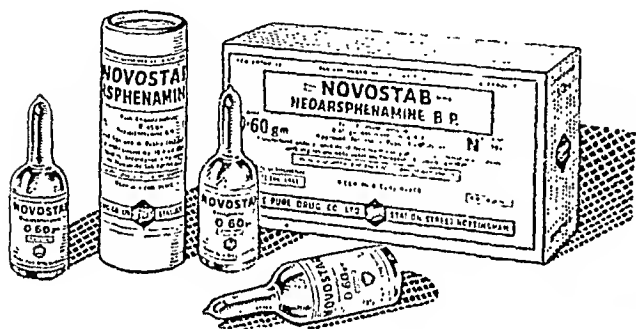
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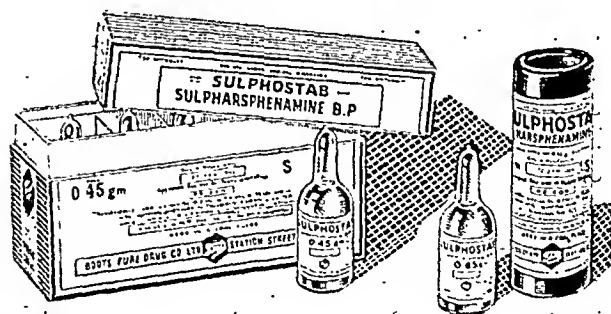
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inch from the cut end. This is tied, and is subsequently used for drawing the ureter into the lumen of the bowel and for fixing it to the bowel wall. The ureter is now turned backwards over a pad of gauze; this kinking is enough to prevent the escape of urine. A few interrupted sutures draw together the edges of the incision in the posterior parietal peritoneum.

The position of the incision to be made in the bowel is now determined by finding out where the ureter lies most comfortably against it without kinking. The aim is to carry the ureter obliquely into the bowel in the same alignment as it occupies in its retroperitoneal bed. The site for the right ureter will probably be in the lowest part of the sigmoid or the uppermost end of the first part of the rectum. The actual incision in the bowel will usually be  $\frac{1}{2}$  or 2 in. long, and this is marked out by guide sutures. The incision is made obliquely through the muscular wall down to the submucous layer. The edges will retract, but this process may require to be helped by gently spreading with dissecting forceps or a few touches of the knife, used with the blade on the flat. At the lower end of this oblique bed a small hole is made into the bowel lumen. The idea is to make such an aperture as will comfortably admit the ureter, but in practice it usually works out a good deal larger. Both ends of the stitch on the ureter are now threaded on a small round needle, which is passed through the hole into the bowel and out through the whole thickness of its wall half an inch beyond the aperture. The ureter may have to be manipulated through the latter. Both are pulled upon to draw the ureter to this site and well up against the inner surface of the bowel. The ends are then tied firmly, but not so tightly as to cut through the tissues. The edges of the incision in the muscular layer are now sewn over the ureter with four or five interrupted stitches. If there has been any doubt about the fixation of the ureter the first muscular stitch takes a bite of its wall. The peritoneum is then drawn together over the first sutures, taking great care to bury the ureter-fixation stitch properly. One or two more than the number of deep stitches will be required. It is particularly important that the stitch nearest to where the ureter enters the bowel should be lax, as it is at this point that obstruction may be caused by subsequent oedema or kinking. If after tying this last stitch the ureter is seen to fill up, the suture is causing obstruction and must be removed. If excretion is going on, the urine should be escaping into the bowel while the anastomosis is being made, and the ureter should never distend. The ends of this last stitch are left long, and are used to anchor the bowel to the cut edge of the posterior parietal peritoneum. In this way at the conclusion of the operation the ureter passes directly from its retroperitoneal bed into the bowel, so that it has no intraperitoneal course. If the second ureter is to be transplanted at once the same steps are taken, but the incision in the bowel wall should be an inch or an inch and a half higher up than the first implantation. After completing the toilet of the peritoneum the omentum should be crowded into the pelvis and the patient brought to the horizontal position for closure of the abdomen. For some three years now I have omitted drainage from the site, but it is a perfectly rational safeguard, and the surgeon need not hesitate to use it. The abdominal wall must be very carefully closed, some through-and-through sutures being used. As a last step a tube about forefinger size is passed into the ampulla of the rectum and fixed to the anal margin by suture. This is to prevent the accumulation of a puddle in the rectum which might encourage infection.

The whole procedure takes from three-quarters of an hour to an hour and a quarter, depending upon whether or not both ureters are transplanted.

#### IMMEDIATE AFTER-PROGRESS AND TREATMENT

There should be no shock and very little upset of any sort. Urine may be discharged into the rectum from the outset, but it is more usual for uresis to be delayed for about six hours. At all events, only if

there is no evidence of secretion by the end of that time should active steps be taken to encourage it. Some patients vomit a good deal and a moderate amount of distension is not uncommon. Such symptoms nearly always clear up as soon as uresis is freely established. I have always avoided the use of enemata, fearing to disturb the site of anastomosis. The patient reaches the ward with a glucose-saline drip *in situ*, and this is continued until there is a free discharge of urine from the rectal tube. When the patient recovers from the anaesthetic, the drinking of hot water is allowed and, in the absence of vomiting or distension, encouraged. It is only in cases with rather poor renal output or in which uresis is delayed that the intravenous sodium sulphate 4.3 per cent is employed.\* The rectal tube should be removed in four days, or earlier if it is much resented. Thereafter there may be incontinence for some days, especially in children, and adults may have very frequent calls—perhaps every hour. But even children acquire rectal control quite quickly, and nearly always by the time they are ready to leave hospital—in three or four weeks. Of course some education is usually necessary, and to this end it may be a help to keep the bed-pan in the bed. A capable and understanding nurse will usually manage to assist even small children to acquire control within this time.

#### COMPLICATIONS

In the early stage anuria, chest troubles, and peritonitis are the only likely troubles. At the end of about a week distension, local tenderness in either iliac fossa, quickening pulse, elevated temperature, and general malaise are very suggestive of intra- or extra-peritoneal infections about the site of anastomosis. Such a condition is grave but not necessarily fatal. In two cases (nos. 4 and 5) a localized abscess formed and after evacuation was followed by urinary fistula, yet spontaneous recovery ultimately ensued; and both patients are now, many years afterwards, alive and well. Some infection of the kidney used to be so frequent as to be looked upon as part of the normal convalescence, but in more recent years it has seldom occurred, possibly owing to the simplification of the technique. Most cases turn out to be mild, but, even so, the onset may be rather alarming and attended with considerable general disturbance. As a rule this soon settles down, leaving a swollen tender kidney with some fever as the only indication. In the more serious types things go from bad to worse until the patient presents the picture of acute ascending pyelonephritis, but I have not seen death from this cause for some years. In his anxiety and apprehension about possible renal infections the surgeon must not forget that these patients are liable to the occasional complications attending on laparotomy for any purpose. I have successfully dealt with a case (no. 3) in which a loop of small intestine escaped through the wound and became strangulated, and the burst wound is not unknown.

#### MORTALITY

The mortality rate depends to a considerable extent on the condition demanding the operation. In the non-malignant cases, and especially the congenital deformities it should be very low—perhaps 5 per cent—but in the malignant cases such a low rate is not to be expected if the possible advantages of the operation are to be offered to the greatest number of sufferers. In children some deaths have been due to chest complications and to the exanthemata, and I would stress the wisdom of choosing the summer months for the ordeal and of keeping children in hospital for a fortnight before operation.

#### WHEN TO TRANSPLANT THE SECOND URETER

There is no stated time for dealing with the second ureter, and the interval must depend on the progress

\* 42.85 g. of hydrated sodium sulphate (Glauber's salt) dissolved in one litre of distilled water gives an isotonic solution of 4.3 per cent.

made after the first intervention. If all goes perfectly well, three weeks has proved a proper interval; should it be otherwise, the surgeon must bide his time. The only error is to re-operate too soon.

#### SOME LATE SEQUELÆ

If pyelitis is going to develop it usually comes on within a fortnight of the transplantation, but once having developed it tends to recur at varying intervals, perhaps over a lifetime. Hydronephrosis, on the other hand, probably develops over the course of months, and may not give rise to symptoms unless it becomes infected. Quite often it is discovered only because looked for. Calculus formation is not very rare, for it occurred three times among my first 13 patients who lived long enough to develop the condition. The symptoms became suggestive 15 years, 22 years, and 25 years after the original operation. Frequency of rectal micturition has seldom been a constant feature, but it may be an accompaniment of general ill-health. Rectal incontinence for urine is in my experience the most disturbing sequel. Fortunately it is unusual. In spite of painstaking investigation I have been unable to discover the cause, nor have I been successful in treatment. Wearing a rectal tube at night—a large catheter of the de Pezzer type—is a useful palliative measure.

#### SPECIAL GROUPS OF CASES

**Congenital anomalies.**—Of these the commonest is ectopia vesicæ, which is said to occur once in every 50,000 births. The next are the lesser degrees of the same condition, such as complete epispadias in the male and the corresponding anomaly in the female known as subsymphysial epispadias. *The age at which to operate* is an important problem. I consider that the optimum time will occur somewhere between 4 and 6. But it is not so much a question of the number of years but of the condition, and whatever the age the operation must not be carried out until the child is in established good health. Many a child at 4 is better fitted for the operation than others at 6. But it is never too late to consider operation if congenital deformity is the indication, and my friend Mr. Norman Hodgson dealt most successfully with a case of ectopia in a man of 51 who, by a strange irony, had consulted me 30 years previously, only to be told that no operation was feasible. As a rule children do better than adults, and it is surprising how readily they accommodate themselves to the altered physiological condition.

The exposed mucous membrane of the ectopic bladder is a distinct danger, and many examples of the development of epithelioma have been recorded. Quite apart from this risk it is offensive to the eye, may give rise to an unpleasant discharge, and is liable to mild injury and excoriation. In either sex some sort of plastic repair of the affected area is desirable.

With the lesser anomalies the question of marriage is often raised, and even in complete ectopia patients of either sex have sought the consolation of matrimony. The female with a normal partner may prove fruitful, and there is no reason why such marriages should not be happy. There appears to be no special risk in pregnancy, and, since the pubes is constantly separated, labour is often easy (case 2). In the male sexual gratification is said to occur, but neither of my married male patients has as yet become a father. Now that the transplantation is less likely to be attended by sequelæ, I welcome the opportunity of carrying out more careful and complete restoration of the genitalia.

**Separation of the pubic bones.**—In the case of complete ectopia the pubic symphysis is separated to the extent of from 4 to 6 inches, but the bones are connected by a very strong ligament. It is often assumed that such a degree of separation will result in marked disability, but though the thighs are more or less widely separated and the patient walks with a characteristic gait, they are usually quite strong and able to carry out ordinary activities without impediment.

**Other pre-operative problems that may arise.**—Sometimes there is weakness of the anus with incontinence, and on occasions prolapse. If this is associated with some degree of spina bifida and perhaps weakness of the lower limbs no improvement can be expected, and transplantation into the usual site is contra-indicated. Confronted with these circumstances Hey Groves made the transplantation into the cæcum, and combined this with a left inguinal colotomy. As a result not too frequent pulpaceous stools could be easily controlled by a colotomy belt, and for some years the patient was able to lead a sheltered but useful life.

**Contra-indication to transplantation.**—Marked pyelitis and pyonephrosis are usually regarded as contra-indications to transplantation. It is always worth while establishing external loin drainage by nephrostomy and, if sufficient improvement follows, to proceed to transplantation while the drainage is still operating.

#### THE WIDENING SCOPE FOR TRANSPLANTATION

For many cases of malignant disease of the bladder total cystectomy holds out the best prospect of long palliation or even cure. In this operation it is necessary to divert the urine, and by far the best plan is to carry the ureters into the bowel. The technique is the same as that used in other cases. When the transplantation is a proved success—and this is usually assured in three or four weeks—the removal of the bladder may be carried out.

In some cases of malignant disease of the cervix extension to the adjoining bladder renders treatment both by radium and by hysterectomy impracticable. In such cases total hysterectomy, together with simultaneous removal of the bladder, holds out some prospect, and in the absence of glandular involvement or distant dissemination should be practised. The transplantation of the ureters should be a first stage, and the next part of the operation should not be undertaken until the patient has become stabilized under the new physiological conditions. An interval of 6 to 8 weeks will probably suffice, but there should be no unwarranted haste.

For some years now the operation has been used for certain intractable cases of vesico-vaginal fistula. In such cases transplantation should not be combined with a last desperate attempt at local repair, but should be a deliberate intervention only to be carried out after proper preparation. In the systolic bladder, which is sometimes a problem after the successful removal of a tuberculous kidney, diversion of the ureter into the bowel may bring great relief.

Transplantation has also been used in certain cases of severe injury to the urethra usually associated with fractured pelvis. Though this indication is among the rarest, it should be kept in mind.

#### Recent Advances in the Antiseptic Treatment of Wounds

By L. P. GARROD, M.D., F.R.C.P.

(From the *British Medical Bulletin*, Vol. I, May 1943, p. 48)

THE immense achievements of systemic chemotherapy almost overshadow all other forms of medical progress in the past few years. Yet it will not have escaped the notice of any acute observer that a similar revolution is now taking place in the sphere of local chemotherapy. Antiseptics have been out of fashion since the last war, when they were generally considered to have failed. The orthodox attitude to them has been that they do more harm to tissues than to bacteria, and many surgeons believed that they could neither prevent infection in a wound nor cure it; indeed, in view of this widely held belief it is surprising that antiseptics have been so generally used. Recent observations, of which the following is an account, have rendered this attitude untenable, and there is a prospect that local chemotherapy will improve to the same extent as systemic.

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In 1911, the late Professor Thompson, of Dublin, established that Bovril had the power of ministering to nutrition by the assistance it gave to the assimilation of other foods. Recently a remarkable series of experiments has been conducted at an English University. A group of medical students volunteered to undergo the unpleasant experience of allowing the passage of an œsophageal tube into the stomach so that accurate studies might be made of the effect of certain beef preparations. One of the substances investigated was Bovril.

As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

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## LOCAL SULPHONAMIDE TREATMENT

For five years after the introduction of the sulphonamides the nature of their action was unknown. German and French authors, including Domagk (1937) himself, hotly denied that they had any useful direct action on bacteria at all, and had this belief not been overthrown there would have been no inducement even to attempt their local application. We owe our present knowledge on this fundamental question of Fildes (1940) and Woods (1940), who showed that the action of sulphanilamide on hæmolytic streptococci is to prevent the utilization of para-aminobenzoic acid, a previously unrecognized essential growth factor, and that the action of mercury perchloride on bacteria is of exactly the same nature. That this type of reaction wholly explains the action of sulphonamide compounds generally in all bacterial infections is beyond doubt: it is only necessary that there should be a certain excess of the drug over the amount available of the substance essential for growth, and bacterial growth will cease. Since the concentration of the drug attainable by local application is much greater than that produced in the tissues by systemic administration, the former method should succeed. That it does so is now a matter of general experience.

There are records of several earlier attempts to apply sulphanilamide locally, but the first systematic study of its action in wounds was made by Jensen, Johnsrud and Nelson (1939) who, by introducing quantities up to 15 g. into compound fracture wounds, greatly reduced the frequency of infection in them. To trace the development of this form of treatment since it was given a rational basis by the work of Fildes is unnecessary: it is now common practice, and has been found useful in the peritoneum, nose, ear and elsewhere, as well as in wounds. Preventive treatment, as would be expected, is much more successful than curative, and the conditions against which the safeguard afforded is surest are hæmolytic streptococcal infection and gas gangrene. Hawking's (1941) study of prophylactic effect in experimental gas gangrene gives valuable data on the persistence of the powder in the wound and the concentration attained, both of which depend on the solubility of the drug.

	Concentration in wound fluid	Persistence
Sulphanilamide	1,500 mg. per 100 cm.	Less than 1 day
Sulphathiazole	104 " " "	5 to 6 days
Sulphapyridine	42 " " "	7 to 10 "

Of these three compounds, sulphathiazole best combines adequate dissolved concentration with duration of effect. It is this persistent action achieved by the use of a slowly dissolving solid, which secures effective antiseptics.

The success of this treatment has brought about a complete *volte-face* in the surgical attitude to antiseptics generally: scepticism has given place to receptivity, and where one method has succeeded, others both old and new are now given a fair trial.

## PROFLAVINE

Among antiseptics available as long ago as the last war, acridine compounds had a unique claim to consideration as wound prophylactics. Not only did they combine a powerful though slow action on bacteria with freedom from any gross toxicity to tissues, but they stood alone in having been shown capable of destroying bacteria in experimental wounds and thus preventing infection. The recent revival of interest in these compounds was assisted by Russell and Falconer's (1940-41) observation that a buffered isotonic solution of proflavine was no more damaging to the surface of the exposed brain than normal saline, whereas other antiseptics applied in the same way caused a severe hæmorrhagic necrosis. Proflavine was included in

Hawking's (1941) study, already quoted, of the prophylaxis of experimental gas gangrene, and appears to have been at least as effective as sulphonamides. In the similar experiments of McIntosh and Selbie (1942) proflavine was distinctly more effective than sulphanilamide in preventing the development of *Cl. welchii* infections in mice. Although these recent studies have been concerned only with anaerobes, proflavine is equally effective against pyogenic cocci, and there is no doubt that its introduction into a recent wound should be an efficient method of preventing infection generally.

Clinical evidence of its usefulness has been obtained not by prophylactic use but in the much more difficult sphere of treatment. Mitchell and Buttle (1942) report that the introduction of from 0.5 to 2 g. proflavine powder into intractably suppurating gunshot wounds is often followed by an abrupt cessation of the purulent discharge and rapid healing. Many of their 80 cases had previously had full courses of systemic or local sulphonamide treatment without benefit. It may well be asked why their sensational success should have been achieved with a class of antiseptic which failed to achieve any such striking effect in similar cases during the last war. There are two answers to this question, one of which is the choice of proflavine: the marked superiority of this compound over acriflavine was first emphasized by Albert, Francis, Garrod and Linnell (1938), and strikingly illustrated in the experiments of Russell and Falconer (1940) already quoted. The future of antiseptic treatment with acridine compounds lies with proflavine (2:8 diaminoacridine) and possibly 2:7 diaminoacridine (Albert, Francis, Garrod and Linnell, 1938) and 5 aminoacridine (Rubbo, Albert and Maxwell, 1942): the two latter, which have emerged from the extensive and outstanding work of Albert on the acridines as the most promising among his new compounds, have so far not received adequate clinical trial. The second reason for this success appears certainly to be the method of application. Flavines have never before been used in solid form, and by copying the technique of local sulphonamide treatment, a degree of penetration of persistence has been achieved which is unattainable in other ways. This method deserves general attention and trial.

## PROPAMIDINE

Propamidine (4:4' diamidinodiphenoxypropane dihydrochloride) is one of a series of aromatic diamidines recently introduced for the treatment of trypanosomiasis and other protozoal infections. That they also have a powerful action on bacteria was demonstrated by Fuller (1942), who tested a large number of these compounds on many bacterial species. Even the best of them have apparently no systemic effect on bacterial infections, but the local application of propamidine has given excellent results. The rationale of this treatment is explained by Thrower and Valentine (1943) and three succeeding papers in the same journal describe its clinical effects. Propamidine is applied to wounds in a concentration of 0.1 per cent in a water-soluble jelly base, the cavity being filled with this or the surface covered with a layer of it, which is then covered with vaseline gauze to prevent escape or evaporation. Application is renewed every two days and the treatment continued for not more than ten. The object is to overcome established sepsis, and this has been achieved when treatment with sulphonamides had previously failed. The scope and effects of propamidine treatment are thus almost identical with those of proflavine in the hands of Mitchell and Buttle (1942), and a deliberate comparison of the two methods would be most instructive. Much remains still to be learned about the action of propamidine on bacteria, its nature, velocity, limitations and variability with species. Existing information on the last point suggests that *Streptococcus pyogenes* is the most susceptible species among common wound invaders: *Staphylococcus aureus* is also susceptible, but less so, while *Proteus* and *Ps. pyocyanus* are resistant.





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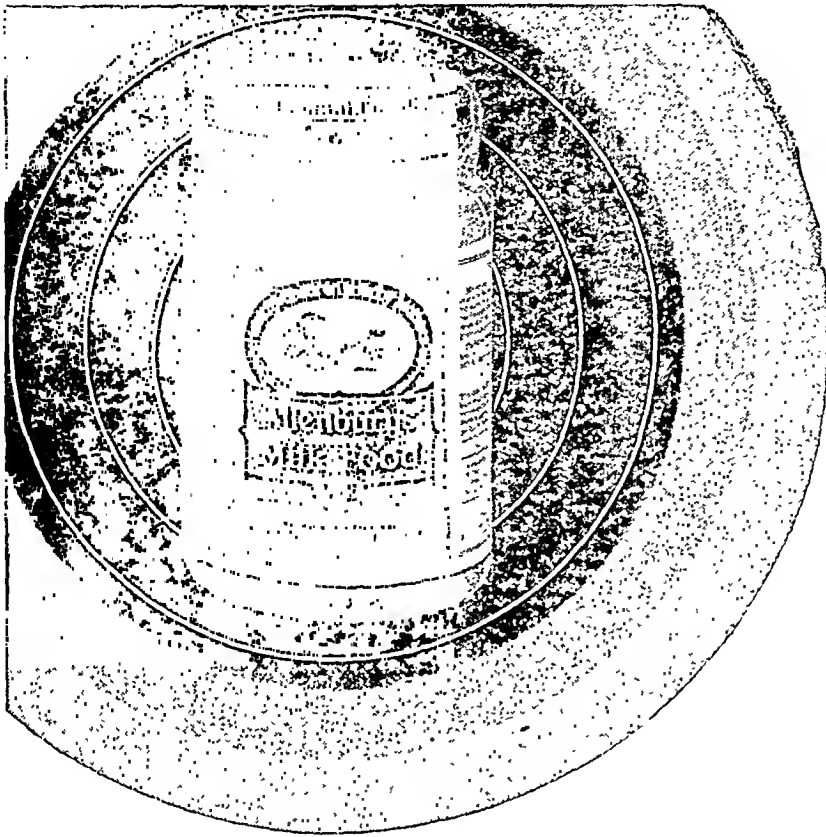
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## Reviews

**A HANDBOOK OF TROPICAL DISEASES: WITH TREATMENT AND PRESCRIPTIONS.**—By J. O. Banerjee, M.B. (Cal.), M.R.C.P. (Lond.), and P. B. Bhattacharya, M.B., D.T.M. (Cal.). Third Edition. 1943. U. N. Dhur and Sons, Limited, Calcutta (18, Bankim Chatterjee Street, Calcutta). Pp. xiv plus 512. Illustrated. Price Rs. 18 or 28s. (In Great Britain)

THIS book first published in 1934 has now reached its third edition; this testifies its popularity. There are several excellent books on tropical medicine, but they are mostly long, deal with some diseases not found in India and contain a mass of detail on parasitology, etc. Thus there is a real need for a small work devoted chiefly to the recognition and management of tropical diseases prevalent in India. We consider that this handbook will serve to meet this demand.

The present edition contains thirty-four chapters, two appendices and an index. The material and the presentation in the body of the book are good. Many pages have been re-written and extra fresh matter has been added; these have increased the size of this edition by one hundred pages. There are several excellent illustrations. The price of the book is rather high for a popular handbook. The publishers, however, deserve credit for bringing out such a well-printed volume with good paper in war time.

R. N. C.

**SYMPTOMS AND SIGNS IN CLINICAL MEDICINE: AN INTRODUCTION TO MEDICAL DIAGNOSIS.**—By E. Noble Chamberlain, M.D., M.Sc., F.R.C.P. Third Edition. 1943. John Wright and Sons, Limited, Bristol. Pp. viii plus 456, with 346 illustrations, of which 19 are in colour. Price, 30s.

In this edition the book has been subjected to extensive revision and includes certain additional laboratory and scientific investigations and a chapter on radiology. It is an excellent introduction to medical diagnosis. The technique of examination and of eliciting physical signs is described, and an account has been given of the common symptoms and physical signs of disease, the aim being to help the student in forming a composite picture of the pathological change in the body, or in other words in making a diagnosis. The book will benefit students entering the clinical course of their study as well as practitioners who wish to refresh their memory. The illustrations which abound greatly enhance its value.

R. N. C.

**MEDICAL RESEARCH COUNCIL. SPECIAL REPORT SERIES NO. 244. CHRONIC PULMONARY DISEASE IN SOUTH WALES COALMINERS.** 1943. Published by His Majesty's Stationery Office, London. Pp. xi plus 222. Illustrated. Price, 10s. 6d.

In 1936 the Medical Research Council undertook an investigation of chronic pulmonary disease in South

Wales coalminers, the whole scheme of inquiry being put under the direction of the Committee on Industrial Pulmonary Disease. The first report, which was published a year ago, dealt with the results of medical survey and pathological studies of the disease, the most important causative factor being found to be prolonged exposure to airborne dust. The second report of the Committee which forms the volume under review deals with the environmental factors which may play a part in the causation of pneumoconiosis as this disease is encountered in the South Wales coalfield, and is mainly devoted to a consideration of the nature of the dust to which the miner is exposed while at the coalfield, the composition of the strata from which the dust is derived, etc. Detailed reports of these investigations are presented in the volume which also includes recommendations made by the Committee with a view to diminishing the pneumoconiosis hazard.

R. N. C.

**AN X-RAY ATLAS OF SILICOSIS.**—By Arthur J. Amor, M.D. (Lond.), M.Sc. (Wales). Second Edition. 1943. John Wright and Sons, Limited, Bristol. Pp. viii plus 206. Illustrated. Price, 30s.

THIS is the second edition of this useful book, portions of the first edition having been lost by enemy action.

The author points out that most textbooks of medicine devote but little space to industrial medicine and that in recent years the cost in life and disability from occupational diseases has become a serious problem to those concerned.

Further as pointed out in the foreword by Sir Wilson Jameson it was not until 30 years ago, when radiological methods were applied to the study of the lungs, that precise diagnosis of these conditions became possible. There was much confusion between 'miner's' phthisis (i.e. silicosis) and pure tuberculous phthisis, and the common mixture of both. Hence the need for a short practical book devoted mainly to the diagnosis of silicosis which this atlas supplies.

In the course of many years' experience amongst the industrial population of South Wales, the author has examined and kept careful records of thousands of workers and so is particularly well fitted to undertake the task.

The book is divided into five sections—I. Introductory Notes and Aetiology. II. The Pathology of Silicosis. III. The Radiological Examination of the Lungs. IV. Clinical Manifestations. V. Prognosis.

The skiagrams, all of which are of excellent quality, are well reproduced and the descriptive letterpress accompanying them is clear and concise.

Both the author and publishers are to be congratulated on the production of this useful work.

J. A. S.

## Abstracts from Reports

**REPORT OF THE EUROPEAN MENTAL HOSPITAL AT RANCHI FOR THE PERIOD 1ST APRIL, 1942 TO 31ST MARCH, 1943.** BY LIEUT.-COLONEL M. TAYLOR, O.B.E., M.D., D.P.H., I.M.S., MEDICAL SUPERINTENDENT

'Owing to scarcity of paper and the high cost of printing', Colonel Taylor observes, 'much detail has been eliminated from the annual report'. That is no doubt the reason why it contains very little of interest. During the year the total population of the hospital was 375, and the daily average of patients was 274. Over 50 per cent of the admissions were from Bengal. The death rate was 14 per cent, a large proportion of the deaths occurring in patients suffering from senile dementia. The parole system has, as

formerly, been extensively used, without any untoward occurrence. Schizophrenia formed nearly a third of the mental disorders for which the patients were

treated. The point worthy of special note is the satisfactory increase in number of patients discharged cured and improved.

## Correspondence

### A PLEA FOR A MORE COMPREHENSIVE OUTLOOK ON THE HUMAN BODY

SIR,—I am pleased to read Dr. Sen Gupta's letter in the correspondence columns of the November issue of the *Indian Medical Gazette* commenting on my special article 'A plea for a more comprehensive outlook on the human body', for it encourages me to try and clarify points that may not be sufficiently clear.

Clinical observation from all angles is what is required in a world population so varied in habit and custom as that in which we live. It is indeed partly this variation that makes the study of 'man' difficult, but it is this very variation that appears to be in conformity with the 'Laws of Nature' which seldom permit of the reproduction of two of a kind. Nature is full of experiment, and does not count the cost.

Had man not been fortunate enough to develop the happy combination of hand, eye, and brain, and to specialize in this last, and so annihilate distance, it is possible that isolation would have permitted as many varieties of his species as there are natural geographical isolation barriers; like the nineteen species of the *Cossawaries* in the Pacific Islands, each species as varied in habit as its particular surroundings demand.

That man can subsist on varying diets points to his great adaptability, and this power of varied adaptation is dependent to a great degree on the present imperfect stage in the development of the human alimentary system, for such powers of adaptation are denied to the true ruminants and carnivora whose alimentary systems are already perfected to an optimum and incapable of further modification. The point would therefore appear to support my thesis.

The particular variety of monkey chosen for examination, the *Macacus sinicus*, was selected because it is believed to be a purely vegetarian (herbivorous) variety. As I have remarked, 'this little creature has become almost entirely herbivorous; indeed Dr. Aykroyd tells me that he cannot get this type of monkey to eat meat'. 'It is seen that although the stomach is simple, very like that of man, the large intestine, the cæcum, and the appendix are purely herbivorous'. It did not die because it would not eat meat, but was destroyed because it was out of condition. This is clearly stated; it is incorrect to interpret my statement as Dr. Gupta has, to the effect that 'the unfortunate *Macacus sinicus* who died of enteritis because he would not eat meat'. This reading undermines my whole comparison for it is sketched for the very reason that it represents an alimentary canal that has become entirely herbivorous.

The sketch that I reproduced also makes this idea clear, for I have drawn attention to the voluminous cæcum and colon, showing more morphological similarity to the floating cæcum and double colon of a horse, than to the small cæcum cum appendix and colon of man. And, it has no appendix.

The question that I ask is; is this the direction in which man's alimentary system is developing? I have offered no generalities on the subject of the *Macacus sinicus*, but use it as a picture of man's possible final stage of intestinal development. I hope anyone who has made a similar misreading of this point will re-read the original correctly.

The apes are however mixed feeders and to quote my own expression, 'insectivorous (carnivorous) and seasonal frugivorous'; one is not surprised therefore to find that the apes still have an alimentary system similar to man's, complete with an appendix.

The point raised about the probable value of a high protein diet in tuberculosis cannot be dismissed lightly. The possibility remains, despite the difference of opinion amongst those who have specially studied the subject. It is still possible that the decline in the health and stamina of the North American Indians is due more to the sudden change of diet from that gained by hunting and fishing, to that of modern civilization, than to the exposure of a race lacking in immunity to tuberculosis, for there is good evidence that the population of the Americas was derived from the Far East, a part of the world by no means free from tuberculosis from time immemorial. Moreover the Greenland Eskimos who have continued on their entirely carnivorous diet which includes every part of the animal captured, are said to be entirely free of deficiency, vascular, and renal diseases, while on the other hand, the Labrador Eskimos who have abandoned their carnivorous habits and have adopted a diet of cereals are found to suffer from all the misfortunes of modern civilization.

The point is also raised in the correspondence columns; is man's intestinal canal so unlike that of the horse? Yes, after the stomach there is no similarity, the horse has a relatively huge small intestine, a voluminous cæcum that has a capacity of some sixteen gallons, an equally voluminous double colon, and vestige of an appendix. Man can survive without any of his colon? Could a horse?

As regards my challenge of the universal belief that milk is a perfect article of food for any animal except the young. The cow and goat are dairy animals, not by the Laws of Nature, but by the artefact of man, it is one of the examples of the developed brain turning environment to needs. That dairy produce is desirable and pleasant needs no defence, but is milk a digestible article for the adult? In answer to this Dr. Gupta has the vast majority on his side, nearly all doctors, and therefore farmers and big business who advertise, but when I carry out the experiment suggested by Dr. Gupta and mix warm milk with rennet in one vessel, and warm milk with 2 per cent HCl and pepsin in another, I notice the difference between a junket and a mixture of curds and whey as readily as any housewife.

That the produce of the earth will support a greater population than a purely meat diet is obvious, and that the greater portion of man's diet must henceforth be grain is equally obvious, hence the valuable work of skilled scientists and dieticians who seek to find an optimum that will be both sufficient in all proportions and economical for the masses, but if the clinical observation be upheld that man is altering his environment quicker than nature can modify structure, then such observation may be of value to these scientists, for remember, from my diagrams, man's alimentary canal has already entered into the transition stage from an insectivorous (carnivorous) and seasonally frugivorous type towards the herbivorous type. For example, it may prove possible in the future, should the experiment be pursued, to cultivate *in vitro* the symbiotic bacillus that stores nitrogen in the roots of leguminous plants as swellings, and in this way utilize the nitrogen of the air as a substitute for meat in much the same way as yeast can be made from molasses, for yeast is mostly nitrogen but unfortunately very unpalatable.

That man can live and grow strong on a purely grain diet depends on many factors, chiefly exercise and fresh air to metabolize excess of sugar. A labourer can live without suffering from the disabilities that

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☆ The details given are of an actual case. The illustrations are made from photographs taken of this case.

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## HANDBOOK OF PHYSIOLOGY AND BIOCHEMISTRY

By the late W. D. HALLIBURTON, M.D., LL.D.,  
F.R.C.P., F.R.S.

Formerly Professor of Physiology, University of  
London, King's College

and

R. J. S. McDOWALL, M.D., D.Sc., F.R.C.P. (Edin.),  
Professor of Physiology, University of London,  
King's College.

**THACKER SPINK - - CALCUTTA**

I have mentioned for the reason that his physical labour uses up his vast store of glycogen, but reference to my article in the *Indian Medical Gazette* of November 1941, will show that he too suffers from hypoproteinaemia and disability consequent thereon. The Chinese 'giant killers' who are rationed with 26½ ounces of rice a day will fully utilize this amount while fighting, but on return to peace conditions I doubt not that they will expect a little variation in the form of mutton and fish. It has long been recognized that the diet of a man doing hard work should contain more carbohydrate than that of the sedentary worker, and it is the sedentary worker who suffers mostly from the ills of too much starch.

That a diet rich in protein is a cause of sadism is certainly debatable, I should rather think that this is due to early training and mental development, for where reason is highly developed there is no possibility of cruelty. It is possible that a pure vegetarian can, if provoked, be as ferocious as any, the African Bison certainly is.

Now, the writer is not despondent, for he believes that *homo sapiens* will justify his name in time, for having developed a brain he will study, and find, that he can mould environment to his needs, and where environment and or habit is found to be faulty, bring about the necessary change. What man cannot do, is to bring about anatomical and physiological changes in his alimentary system to suit the poorly prepared environment in which he finds himself to-day.

I gather that Dr. Gupta is a vegetarian. If so I hope he has not missed the compliment implied in my thesis, namely that he has already achieved the goal towards which I suggest that all mankind is heading as regards his *alimentary system*; the goal achieved by the *Macacus sinicus*? This all shows that good health and long life are possible for a vegetarian as we all know from experience, it also shows that an imperfectly adapted species can be very successful though the imperfection of the adaptation may lead to much individual suffering, which may well, by understanding and individual study, be avoided.

I think that I should also call attention to my remark that 'Man can subsist on either or both diets, the Esquimo being wholly carnivorous, and many in this country being wholly herbivorous, a mixed diet rich in protein being generally acceptable'; for it appears possible that some readers consider the writer to be an advocate of a purely meat diet which would not be in conformity with my diagram of Man's intestinal canal which shows a departure from the truly carnivorous and frugivorous in favour of the truly herbivorous type.

A. I. COX,

LIEUTENANT-COLONEL, I.M.S.,  
District Medical Officer.

THE NILGIRIS,  
OOTACAMUND.

## Service Notes

### APPOINTMENTS AND TRANSFERS

THE VICEROY AND GOVERNOR-GENERAL has been pleased to make the following appointments on His Excellency's personal staff :—

To be *Honorary Surgeons*  
9th August, 1943

Colonel R. Hay, C.I.E., *vice* Major-General J. B. Hance, C.I.E., O.B.E., vacated.

20th October, 1943

Colonel W. C. Spackman.

Colonel (Local Brigadier) G. Covell, C.I.E.

Colonel (Acting Brigadier) W. Ross-Stewart, C.I.E.

29th October, 1943

Colonel (Acting Brigadier) J. W. Vanreenen, O.B.E., *vice* Colonel A. C. Macrac, vacated.

Colonel L. Lee, *vice* Colonel (Local Brigadier) R. V. Martin, C.I.E., vacated.

His Excellency the Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's personal staff, with effect from the 6th December, 1943 :—

To be *Surgeon to His Excellency the Viceroy*  
Lieutenant-Colonel H. Williamson, O.B.E., I.M.S. (Retd.), to officiate as Surgeon to His Excellency the Viceroy, with effect from the 6th December, 1943, *vice* Lieutenant-Colonel H. H. Elliot, C.I.E., M.B.E., M.C., granted leave.

Major M. Jafar, Health Officer, Karachi Air Port, is appointed to officiate as Chief Health Officer, Delhi, with effect from the date he assumes charge of the post, *vice* Major C. K. Lakshmanan.

Major C. J. H. Brink is appointed to officiate as Health Officer, Karachi Air Port, with effect from the afternoon of the 11th December, 1943, *vice* Major M. Jafar.

Major B. S. Nat was appointed Medical Superintendent, Irwin Hospital, New Delhi, with effect from the 4th December 1943.

### INDIAN LAND FORCES—INDIAN MEDICAL SERVICE (SECONDED TO THE INDIAN ARMY MEDICAL CORPS) (Emergency Commissions)

#### To be Captains

Julian Norman Joseph Pacheco. Dated 26th August, 1943.

Fazl-i-Haque. Dated 21st September, 1943.

Susai Louis Bernard Peries. Dated 13th November, 1943.

Ramachandra Rao Koty. Dated 14th November, 1943.

15th November, 1943

Shiv. Ram Singh. Sira Srinivasa Rao.

Meenakshisundaram Muttukumarasami.

Puthupparampil Kizhakathil Adima Kasim. Dated 16th November, 1943.

20th November, 1943

Sibaprasad Mitra. Himangshu Jyoti Kar.

Amarendra Nath Mukherjee. Dated 29th August, 1943.

V. O. Sundaram Pillai. Dated 11th November, 1943.

Abdur Rahim. Dated 14th November, 1943.

Kanhaiya Lal Kapur. Dated 19th November, 1943.

Kamleshwari Prasad Dutta. Dated 19th November, 1943.

Muzaffar Ali. Dated 6th October, 1943.

Gopendra Nath Mukherjee. Dated 15th October, 1943.

Asuram Sur. Dated 19th October, 1943.

Ganjigunte Vankatesiah Chandrasekhara Iyer. Dated 15th November, 1943.

Mir Alam Khan. Dated 19th November, 1943.

Balubhai Harishanker Bhatt. Dated 12th October, 1943.

Jai Chandra. Dated 19th November, 1943.

Turuvekere Dharmayya Venkata Krishnan. Dated 20th November, 1943.

The undermentioned officers are transferred to the General Service Cadre, with effect from the date specified :—

Captain S. S. Chhabra. Dated 13th November, 1943.  
Captain N. J. Choksey. Dated 22nd November, 1943.

Captain Santosh Kumar Mitra. Dated 19th December, 1943.

The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service with the Royal Indian Navy :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
(Emergency Commission)

Captain Fazl-i-Haque. Dated 20th December, 1943.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED FOR SERVICE WITH THE INDIAN AIR FORCE  
(Emergency Commissions)  
To be Captains

Bani Kumar Ghose. Dated 23rd September, 1943.  
Mohammad Masudal Haque. Dated 17th October, 1943.

To be Lieutenants

Vithal Sheshgir Joshi. Dated 15th November, 1943.  
Hukam Chand Gupta. Dated 8th July, 1943.  
Michael Deryck Innis. Dated 17th November, 1943.  
Krishnagiri Bheemasena Krishnaswami Rao. Dated 15th November, 1943.  
Subimal Chaudhuri. Dated 20th November, 1943.  
Henry Arthur Garstin. Dated 21st November, 1943.  
George Anthony D'Vaz. Dated 12th September, 1943.  
Behman Sorab Moos. Dated 13th October, 1943.  
Gurmukh Singh Sekhon. Dated 14th November, 1943.

19th November, 1943

Tanwir Mohammad Niaz. Madan Mohan Chauhan.  
Sankar Prosad Das Gupta. Dated 8th November, 1943.

Dilip Kumar Mitra. Dated 10th November, 1943.  
Kali Mohan Bose. Dated 18th November, 1943.

20th November, 1943

Sambhu Nath Datta. Shishir Kumar Ghose.  
Harish Chandra Chakravarti.

30th November, 1943

Prabhat Kumar Bose. Sourindra Nath Sen Gupta.  
Ramendra Nath Dutta.

(WOMEN'S BRANCH)

To be Captains

(Mrs.) Rajrajeshwari Devi Karki Pahwa. Dated 17th November, 1943.

(Miss) Mary Thomas. Dated 8th October, 1943.

Miss Mary Kozhimannil Verghese. Dated 2nd November, 1943.

Mrs. Saralabai Atmaram Kulkarni. Dated 13th November, 1943.

To be Lieutenants

Miss Kidambi Sreenivasa Jaya Lakshmi. Dated 13th November, 1943.

Miss Razia Abdulkader Gulmohamed. Dated 26th November, 1943.

(WITHIN INDIAN LIMITS)

To be Captain

Miss Annamma Abraham. Dated 25th November, 1943.

PROMOTIONS

Lieutenant-Colonel to be Colonel

R. N. Khosla, O.B.E. Dated 31st August, 1943.

Major to be Lieutenant-Colonel

G. J. Joyce. Dated 22nd December, 1943.

Captain to be Major

W. S. Davidson. Dated 23rd December, 1943.

The undermentioned officers (on probation) are confirmed in the Indian Medical Service, with effect from the dates specified :—

INDIAN MEDICAL SERVICE  
(Permanent Commission)

12th May, 1939

Captain D. F. Eastcott.

Captain L. H. Cooper.

Captain A. M. McGavin. Dated 15th May, 1939.

27th September, 1939

Captain W. M. McCutcheon.

Captain G. S. Michelson.

Captain J. Aitken.

Captain P. W. Kent.

Captain R. O. Yerbury.

Captain P. J. Wormald.

Captain G. T. M. Hayes.

Captain J. P. O'Riordan.

Captain H. Rees.

Captain D. S. Wilson.

Captain A. S. Brown. Dated 19th October, 1939:

RETIREMENT

Lieutenant-Colonel J. Carrey, on account of ill-health. Dated 20th July, 1943.

RESIGNATION

INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—(SECONDED TO THE INDIAN ARMY MEDICAL CORPS)

(Emergency Commission)

Captain Balubhai Harishanker Bhatt. Dated 3rd November, 1943.

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## Original Articles

### TYPHUS IN AKOLA (BERAR)

By K. G. PRADHAN, L.M.P., L.T.M.

*City Dispensary, Akola, Berar*

DURING six and a half years' work at Akola, I have seen not less than fifty cases of typhus. The first case was seen in the year 1937 at one village. A fortnight later I saw a fatal case in Akola. Since then, eight to ten cases have been treated every year in the same season, i.e. between August to October. The mortality in these cases was about 10 per cent.

These cases were diagnosed as cases of typhus fever from the following common clinical manifestations :—

(1) A fever of remittent or continuous type of about two weeks' duration, and usually ending by lysis.

(2) The appearance of a rash, macular and hæmorrhagic, on or about the sixth day of fever. In mild cases the rash was papular.

(3) The early toxæmia.

(4) A bronchitis and in some cases broncho-pneumonia.

(5) Albuminuria.

(6) In all cases the temperature came down to normal by lysis except in three in which it had come down by crisis.

All cases were in adults.

The above were the general manifestations in the majority of cases which indicated the diagnosis of typhus. I quote below some details.

(1) *Fever*.—This was as a rule continued or remittent but in one case the temperature was almost intermittent, the morning temperature dropping to 98° daily.

(2) *Rash*.—In the majority of cases the rash appeared on the fifth or sixth day of the fever, in one case on the eighth day and in two cases as early as on the third day. The rash in about 75 per cent of cases was macular and thick, involving the whole of the body excepting the soles and palms. In about 20 per cent of cases the eruptions were discrete, and in all these cases the face, the soles and the feet were free. In both these types of case, the rash persisted for about a week after the temperature had come down to normal. During this period the eruptions went through various colour changes; first pink then dark red, brownish and gradually changing to greenish blue. In 5 per cent of cases the skin lesions were few and limited to the trunk alone, and faded within about four to five days, before the temperature came down to normal.

(3) *Marked toxæmia*.—This was present in all cases with a marked rash (about 75 per cent of cases). It generally appeared on the eighth or ninth day of the disease, and in a few cases as early as the fifth or sixth day, and was always preceded by the red congested appear-

ance of the eyes, and by insomnia. Its manifestations varied from occasional incoherence of speech and slow response to calls, to low muttering delirium. In the 25 per cent of cases with less severe eruptions, the toxæmia was present but was very mild. In these cases the patients appeared to be rather indifferent, and had to be questioned several times to get an answer. In 5 per cent of cases the patients did not complain of anything except sleepiness, and they said they were in bed merely because the doctor said they had fever.

(4) *Respiratory symptoms*.—All cases had bronchitis. The cases with severe rash had severe bronchitis. Some of them had signs of broncho-pneumonia, while others had only troublesome cough with no signs in the lung; in marked cases, lung signs and cough were often absent.

(5) *Albuminuria*.—Except in mild cases, albuminuria was invariably present, and generally appeared on or about the sixth or seventh day of the fever, just a day or two before the appearance of marked toxæmia. In some serious cases, samples of urine were examined for casts, and granular and even blood casts were found. These patients had severe toxæmia and were almost comatose. In these cases the albuminuria was found increasing daily. In mild cases the albumin in the urine disappeared about two to three days before the dropping of the fever. Increasing albuminuria with blood casts in the urine was found to be a bad prognostic sign.

(6) *Temperature*.—Fever lasted for about two weeks in all cases. It was continuous in very severe cases, remittent in less severe cases and intermittent in one case which was very mild. The range of temperature on an average was about 103°F. to 105°F. in severe cases, 100°F. to 102°F. in less severe cases and 98°F. to 100°F. in the very mild case. Temperature records of all the cases are not available.

Two of my own cases were fatal. One had broncho-pneumonia and another died of circulatory failure. In all the cases, splenic enlargement and jaundice were absent.

Unfortunately it was impossible to get serological studies made in these cases. Only one Weil-Felix test was done (at the School of Tropical Medicine, Calcutta) and the result was inconclusive.

The majority of the cases were in poor persons who were found infected with all the three types of lice, but in some cases there was no louse infestation. In some cases, the possibility of tick typhus was considered, since the patients were cultivators. In the year 1937, in a case of a child, the possibility of a jungle tick as a probable insect vector was suggested. It is impossible to say with what type of typhus we are dealing.

I am highly indebted to the Civil Surgeon, Akola, Dr. T. D. Shahani, who took a great interest in these cases and encouraged me to write this note.

## A REPORT ON THIRTY CASES OF TYPHUS FEVER (LOUSE BORNE)\*

By BALBIR SINGH

CAPTAIN, I.A.M.C.

LOUSE-BORNE typhus fever was reported to be prevalent in German armies in Poland, Baltic states and the Ukraine in the latter part of 1941 and in 1942. Early in 1943, this wave of epidemic reached us in 'Paiforce'. Our troops with a few exceptions were not affected because of efficient and rigid prophylaxis. The disease raged in an epidemic form amongst the civilians in certain places. The few cases that we had were amongst those of our personnel that came in close contact with the civilian labour. We will discuss in this paper 30 cases that were admitted to a General Hospital.

These cases could be divided into the following groups as far as the severity was concerned :—

1. Mild .. .. . 3
2. Severe
  - (a) Moderately severe .. 8
  - (b) Severe .. .. . 16
3. Fatal .. .. . 3

*Race incidence.*—No race immunity was seen nor could any relation be established between race and the severity of the disease.

*Age incidence.*—

Age groups	Number of cases
20-30 ..	23
30-40 ..	5
40-50 ..	2

All the mild, moderately severe and severe cases were in the age groups 20 to 40. Both cases in the age group 40 to 50 were fatal. A third fatal case was in a patient aged 27 years. This patient died as a result of complications (staphylococcal infection), rather than the primary disease.

As the majority of our personnel belonged to the younger age groups, we could not conclude that younger people were more susceptible to typhus. It was, however, obvious that typhus was more likely to be fatal in older age groups.

### Clinical conditions in different groups

#### Mild cases—3

The patients were admitted with a complaint of fever. Onset of fever was associated with headache and chill. Examination showed conjunctivæ slightly injected, tongue furred; rash though scanty was visible in one fair-skinned individual, not in the other two who were dark-skinned. Heart sounds were normal; lungs showed rhonchi in 2 cases towards the end of the pyrexia. The spleen and liver were palpable in one. No mental symptoms, which are so characteristic of the severe form of the disease,

were seen. Temperature ran up to 102°F. with a daily remission of 1°F. to 2°F. Fever lasted for 6 to 9 days. Diagnosis could be confirmed with the help of Weil-Felix reaction. Convalescence was fairly rapid. One of the mild cases had been protected against typhus, by Cox's vaccine, three months before this illness.

### Laboratory findings in 2 cases in this group

#### CASE 25

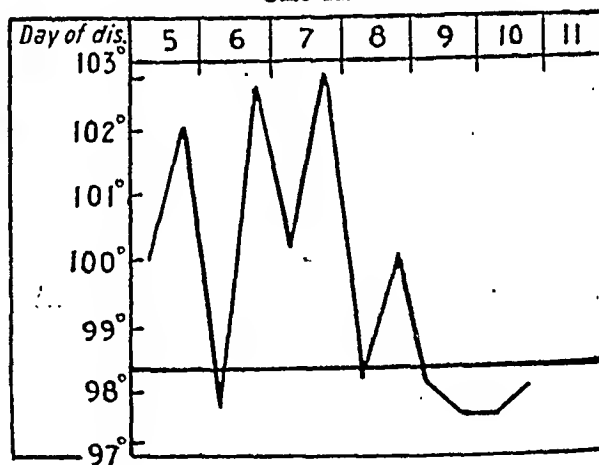
Day of illness	..	6	11	16	22
OX2	..	0	0	0	0
OXK	..	50	50	50	50
OX19	..	125	1,250	500	250
To	..	20	20	0	0
Ag	..	0	0	0	0
W.B.C., per c.mm.	..	9,350			
Polymorphs., per cent	..	67.0			
R.B.C., per c.mm.	..	4,900,000			

#### CASE 17

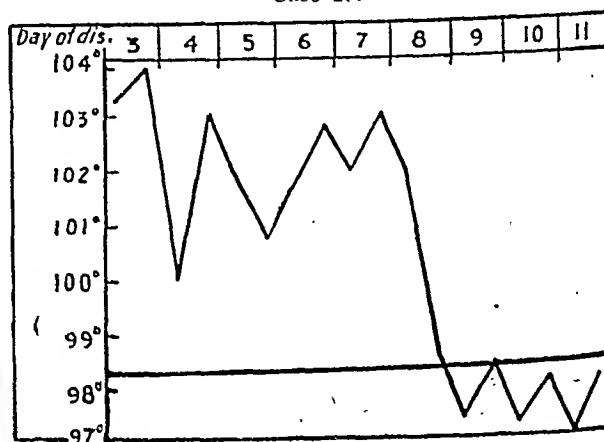
Day of illness	..	6	8	14	16
OX2	..	50	125	500	500
OXK	..	50	50	250	125
OX19	..	50	250	125	125
To	..	0	40	40	0
Ag	..	0	0	0	0
R.B.C., per c.mm.	..	4,400,000			
W.B.C., per c.mm.	..	8,750			
Polymorphs., per cent	..	62.0			
B.S.R., mm.	..	18			

Temperature normal from the 9th day.

Temperature charts of mild cases.  
Case 14.



Case 17.



\* This article was written when the writer was working as a Pathologist in Persia-Iraq Force.

*Moderately severe cases—8*

These cases were admitted with a complaint of fever and cough. Onset of fever was associated with headache, pains in the body, and chill; thirst and soreness of the throat in some. Conjunctivæ injected; became more marked with the progress of the disease. Tongue coated brown and dry. Rash could be observed easily in 4 to 6 days. Two cases that did not show a rash had a definitely dark skin. Rash was pink, macular and more marked on the axillary folds to begin with, extending to the chest, back, thighs and legs by the 7th day. Hands, feet, neck and face were free from the rash in this group. Rash became deep red and later on bluish-red. It started disappearing in the middle of the 2nd week and left behind a brown staining of the skin which could be noticed for another week or two.

The spleen was palpable in 3; malaria parasites (B.T.) were present in 2 cases.

Heart sounds were normal in the first 5 or 6 days. They were feeble in the 2nd week. Pulse rate rapid and weak in the 2nd week. Lungs showed rhonchi. Crepitations were present at the bases in the 2nd week but no definite signs of broncho-pneumonia.

Mental symptoms. There was drowsiness by the end of the 6th or 7th day, mental confusion, difficulty in answering questions and lack of interest in surroundings; short bouts of low muttering delirium or excitement.

Temperature varied from 101°F. to 104°F., usually remittent with a daily remission of 1°F. to 4°F. Maximum temperatures were less in the 2nd week. Intermittent temperature in the 1st week in one case only. Most cases showed intermittent temperature during the last 2 to 4 days of the pyrexia. Defervescence by the middle of the 2nd week.

Average duration of pyrexia in this group was 14 days.

One case in this group had been protected against typhus by Cox's vaccine 1½ months before the onset of the disease.

*Laboratory findings in 2 typical cases*

## CASE 5

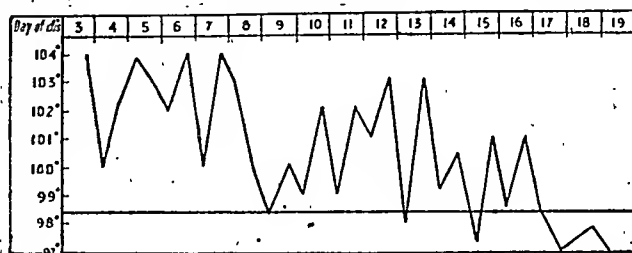
Day of illness	8	11	15	65
OX2	0	50	125	25
ONK	50	250	500	125
OX19	25	250	500	50
To	80	40	20	nil
Ao	20	nil	nil	nil
W.B.C., per c.mm.	10,000	9,800		
Polymorphs., per cent	70.0	56.0		

## CASE 1

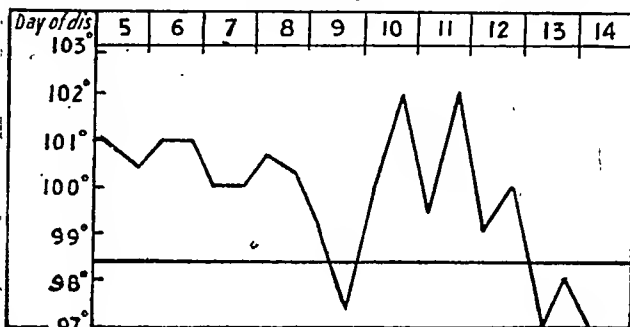
Day of illness	13	17	23	31	61
OX2	500	1,250	500	500	50
ONK	2,500	2,500	2,500	2,500	50
OX19	1,250	1,250	2,500	500	50
To	320	640	160	160	160
Ao	20	20	20	20	20
W.B.C., per c.mm.	6,800				
Polymorphs., per cent	78.0				

## Temperature charts of moderately severe cases.

## Case 5.



## Case 1.

*Severe non-fatal cases—16*

Admitted with a complaint of severe headache (especially frontal), pains in the body, referred to the joints especially in one case, fever and cough of 3 to 7 days' duration. Some of them felt very thirsty and had sore throat.

The disease in this group was severe enough to make the sufferers seek admission earlier.

Face was flushed in some cases.

Conjunctivæ showed marked injection from the beginning. Sub-conjunctival hæmorrhages developed in 2 cases, early in the 2nd week.

Mild deafness was present in most cases by the 4th or 5th day. Three cases took more than a week after convalescence had set in to recover from this.

Thick brown coating of the tongue was present; increased as the disease progressed. The tongue was dry and cracked in the 2nd week. Difficulty in protrusion and tremors were present. Sordes collected on the teeth and lips; these dried up with the progress of the disease.

Pharyngitis. Hoarseness was very marked in 2 cases. Both recovered their normal voice 10 days after the convalescence had set in.

Rash distribution was as described in the last group.

It extended to the face in one case and to the thenar eminences of three cases. Rash simulated that of measles very much in the case in which it extended to the face. It was more profuse and sometimes maculo-papular. Some of the spots disappeared under pressure but others did not. In severe cases it tended to be petechial.

Eleven out of 17 cases in this group showed palpable spleen. It was soft in most cases; tender on palpation in one case.

Heart sounds were feeble within 4 to 5 days of the onset. Became weaker in the 2nd week.



No adventitious sounds. Pulse rate rapid and proportionate to the temperature except in one case where it was relatively slow, weak in force and poor in volume. Weakness increased with the progress of the disease.

Skin and lips showed cyanosis in severe cases.

Blood pressure. The consensus of opinion amongst the medical officers in charge of the cases was that it fell distinctly by the end of the 1st week. There is a record of only 4 cases available with me. Three of them showed a distinct fall in systolic as well as diastolic pressure.

Mental symptoms developed earlier and were much more marked in this group; drowsiness by the 3rd or 4th day of the illness, mental confusion, bouts of delirium made their appearance by the 5th or 6th day. Restlessness and insomnia were present if hypnotics were not administered. Twitchings of the muscles were seen in some cases. A state of coma vigil appeared in very severe cases. There were occasional bouts of excitement in 2 cases. One complained of sensation of flies crawling over the body when he moved in bed.

Mental symptoms were observed by a colleague in another general hospital (personal communication from Captain Bushnam, I.A.M.C.).

One of his patients was found missing from his bed. He was traced out in a building about a furlong from the hospital. The mental condition of this patient later deteriorated very much. The Weil-Felix reaction was positive in this case. Another patient whom they had labelled clinically as typhus was found wandering three miles away from the hospital. The mental condition cleared up gradually after defervescence.

Some of the patients were seen lying motionless in their beds for a couple of days after the temperature had become normal, with their mouths gaping and eyelids closed. They appeared unconscious, as they did not bother about the flies sitting on their faces. They replied when addressed but their reply expressed resentment at interference. They would fall back into the same posture again after replying. It took them a week before their mental processes were normal. Some were very hilarious during convalescence, and these were extremely happy about escaping almost from the jaws of death.

Tremors. Tongue showed tremors from the end of the 1st week in most cases. Well-marked tremors of fingers and hands were present in one case three weeks after convalescence had set in.

Cirriping was complained of by one; diarrhoea with exudate was found in one; vomiting was met with frequently.

Retention of urine was seen in 2 cases. Albumin, a trace, was present in the urine of all cases in the 2nd week. Microscopic examination of urine was not done as a routine. Three cases were however recorded to have shown R.B.C. in urine.

The temperature was remittent; the maximum daily rise 104°F. to 105°F. in the 1st week in 2 cases. It then gradually came down from the peak in 4 days' time and was intermittent for 4 days before becoming normal. Average duration of pyrexia in this group was 17 days.

#### Laboratory findings in 2 typical cases

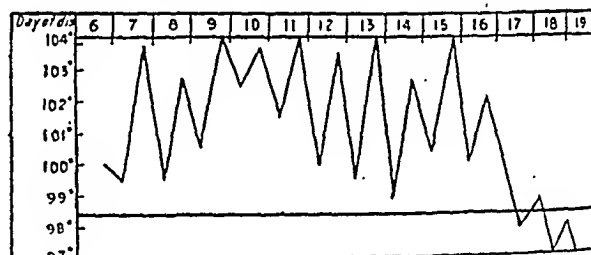
CASE 22				
Day of illness	..	7	12	16
OX2	..	25	125	125
OXK	..	50	250	250
OX19	..	500	5,000	5,000
To	..	0	0	0
AO	..	0	0	0
R.B.C., per c.mm.	..	4,500,000		
W.B.C., per c.mm.	..	4,500		
Polymorphs., per cent	..	70.0		
B.S.R., mm.	..	19		

Temperature came down on the 16th day. Could not be examined after that.

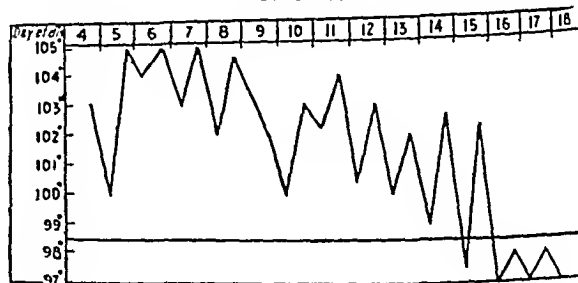
CASE 4					
Day of illness	..	9	14	19	24
OX2	..	50	500	2,500	1,250
OXK	..	N.A.	2,500	5,000	2,500
OX19	..	0	2,500	2,500	2,500
TO	..	80	80	80	80
AO	..	0	0	0	0
W.B.C., per c.mm.	..	6,000			
Polymorphs., per cent	..	60.0			
R.B.C., per c.mm.	..	4,500,000			
B.S.R., mm.	..	23			
Urine	..	R.B.C., in large numbers.			
Temperature normal on the 18th day.					

#### Temperature charts of severe cases.

Case 4.



Case 23.



Case 27

#### A severe case with a complication of streptococcal empyema

The patient complained of frontal headache and fever of a week's duration for which he had quinine before admission. On admission (7th day of illness), temperature 101°F. and P/R 88/22. Tongue coated and moist; breath foul. Looked very ill. Pink macular rash was present on axillary folds, abdomen, and chest. A few spots on the arms and thenar eminences. Heart sounds were feeble. Blood films showed a few M.T. rings.

He became drowsy and his pulse was weak by the 9th day of his illness. His tongue gradually became more coated and tremulous. Rash became more prominent. Face, legs and soles of the feet remained unaffected. Petechial hæmorrhages developed at pressure points and they coalesced into large discoloured areas on the knees above the patellæ. Had a rigor for 15 minutes on the 11th day of his illness. Rash commenced fading and left behind brownish subcuticular staining. He was still drowsy on the 13th day. Had difficulty in protrusion of the tongue, and fingers showed fine tremors. Respiration became laboured on the 14th day and by the 16th day his right base showed dullness on percussion, diminished air entry and crepitations. Had hæmoptysis on the 13th day—it continued up till the 30th day. His mental condition improved after the 16th day. A skiagram on the 18th day showed relative radio-opacity in left mid-zone. Heart shadow was increased. Area of dullness increased in size by the 21st day. He was running evening temperature (maximum rise to 102°F.) and had become very weak and emaciated. A skiagram on the 27th day showed increase of the radio-opaque shadow and it was denser than before. Hæmoptysis disappeared by the 32nd day. Crepitations at the base had diminished but breath sounds were still bronchial.

Diagnostic exploration of the chest on the 35th day showed pus cells and *streptococcus B. hæmolyticus* in the fluid aspirated. No acid-fast bacillus grew on egg-gentian-violet medium. He made remarkable improvement on M&B 693. He had not fully recovered when I had to leave the hospital.

Titre was the same as for OX19 in 9 cases. In 14 cases it was less than that of OX19. Highest titre recorded with OXK was 5,000. It was only 125 in a fatal case where OX19 was 25,000 and 50 in another fatal case whose OX19 was 5,000.

(iii) OX2—Titre OX2 was low when compared with those of OXK and OX19. Sixteen cases showed OX2 from 0 to 250 whereas only 3 cases had titre below 500 with OX19. Maximum titre recorded for OX2 was 2,500 in one case only, whereas 12 cases had shown titre of 2,500 or more with OX19. Titre of OX2 was double of OX19 in 3 cases. Maximum titre recorded in each of these 3 cases was OX2,500.

Weil Felix at the end of convalescence (50 to 65 days) in 6 cases.

	TITRE DURING ILLNESS		TITRE AFTER CONVALESCENCE (50 TO 60 DAYS AFTER THE ONSET)	
	Lowest	Highest	Lowest	Highest
OX2 ..	50	500	0	50
OXK ..	500	2,500	50	250
OX19 ..	500	5,000	25	125

#### Laboratory investigations in the complicated case

Day of illness ..	7	11	17	26	37
OX2 ..	0	125	500	250	250
OXK ..	0	0	0	0	250
OX19 ..	50	500	1,250	1,250	2,500
To ..	80	40	0	0	0
Ac ..	0	0	0	0	0
W.B.C., per c.mm. ..	5,000	4,000	6,250	6,400	9,375
Polymorphs., per cent ..	63.0	62.0	60.0	68.0	75.0
R.B.C., per c.mm. ..	5,000,000	5,740,000			
Hb. per cent ..	95.0				
M.P. ..	M.T. rings a few.				
B.S.R., mm. ..	4	6	38	95	105
Urine ..	R.B.C. nil.				

#### Summary of the laboratory investigations

##### 1. Weil Felix.—

(i) OX19—Earliest diagnostic rise of titre was observed in 2 British soldiers on the 4th day of the illness. They showed OX19 to 250 and 500 respectively. A Persian civilian showed OX19 to 250 on the 5th day, and an I.C.R. (Amir Zaman) on the 6th day showed OX19 to 500. Eight cases had a diagnostic rise of titre (varying from 250 to 2,500) from the 7th to 9th days. Eighteen cases showed a diagnostic rise of titre from 10 to 16 days.

Maximum rise of titre was recorded in

4 cases ..	1st half of 2nd week.
7 " ..	2nd " " 3rd "
12 " ..	1st " " 3rd "
7 " ..	From 19 to 26 days.

Highest titre varied from 500 to 5,000 whenever tests could be put up regularly every 4th or 5th day until a week after defervescence. Titre was always high in severe form of the disease. It was 25,000 in a fatal case.

(ii) OXK—Titre for OXK was not tested in 6 cases as the emulsion was not available.

Titre showed a gradual fall in those cases which were examined during convalescence.

2. *Widal* was put up in every case; one case showed 200 per cent rise in the titre for To but it was not sustained.

3. *Total R.B.C. counts*.—Recorded in the 1st week in 8 cases only.

Highest R.B.C. count ..	5,100,000 per c.mm.
Lowest R.B.C. count ..	4,570,000 " "

4. *Total leucocyte counts*.—Recorded in 20 cases only.

Highest count ..	10,000 per c.mm.
Lowest count ..	3,752 " "

Below 4,000 in one case.

Above 9,000 in two cases.

Average count ..	5,776 per c.mm.
Average polymorpho-nuclear count ..	71.0 per cent.

5. *B.S.R.* (pipettes improvised after Westergren were used).

Average B.S.R. in 5 cases in the 1st week ..	15 mm.
" " " 5 " " " 3rd " ..	38 mm.
" " " 5 " " " 9th " ..	12 mm.

It was 70 mm. at the end of the 1st week in a case that proved fatal 5 days later. It

steadily rose to 105 in a case that developed empyema (streptococcal).

6. Blood cultures negative.

*Brief notes on 3 fatal cases\**

*Case 1.*—A male, aged 24 years, was admitted with fever of 3 days' duration. The blood findings made during the illness are recorded below :—

Day of illness	..	7	12	16	31
OX2	..	50	125	500	125
OXK	..	0	..	..	250
OX19	..	0	250	250	125
To	..	20	20	..	..
Ao	..	20	20	..	..
W.B.C., per c.mm.	..	5,800	13,500	..	8,750
Polymorphs., per cent	..	68	72	..	70

Abnormal clinical findings were that there was no rash and no tremors, that the pulse rate was proportional to the temperature, that the fever continued for 39 days but delirium ceased after the 12th day, that retention of urine was present and that catheterization was necessary. At different times during the illness definite but variable signs became detectable in the chest. Diarrhoea with blood and mucus became a marked symptom from the 19th day. At one phase of the illness liver enlargement appeared, and treatment for amoebic hepatitis was given. He died on the 39th day and the post-mortem findings indicated the presence of three infections: a tuberculous pleurisy, a typhus infection, and later a staphylococcal infection with pelvic abscess, lung abscess, empyema and staphylococcal bacteraemia.

*Case 2.*—A male, aged 45 years. This was a fairly typical case of typhus except that the rash appeared late. Definite signs appeared in the lung on the 12th day; tremor of the tongue and difficulty in protrusion on the 13th day; pulse became rapid on the 15th day; deafness from the 16th day; difficulty in swallowing and mental changes marked from the 17th day; death occurred on the 20th day. The blood findings were as follows :—

Day of illness	..	13	20
OX2	..	..	25
OXK	..	..	50
OX19	..	25	5,000
To	..	..	20
Ao	..	..	..

*Case 3.*—The patient was admitted with fever and headache of 5 days' duration, cough and epistaxis of 3 days' duration. The rash was present, and the clinical picture was typical of typhus. From the 6th day the toxæmia became marked; deafness and mental dullness occurred, the pulse became feeble and the rash became more prominent, and petechial hæmorrhages occurred in the skin. Later two large hæmorrhagic patches appeared, one on the left side of the chest and one on the buttock. The patient became delirious, developed incontinence, later coma and died on the 13th day, the signs in the lung being marked before death. The findings of the blood examination were as follows :—

Day of illness	..	8	12
OX2	..	50	500
OXK	..	25	125
OX19	..	50	25,000 (trace)
To	..	20	40
Ao	..	..	..
W.B.C., per c.mm.	..	5,800	..
Polymorphs., per cent	..	71.0	..
B.S.R., mm.	..	70	..
Blood culture	..	Sterile	..

\* Condensed by the editor. The diagnosis of typhus in the first case appears to be rather open to question.

## TYPHUS IN THE UNITED PROVINCES OF INDIA

BEING A CONTRIBUTION TO THE STUDY OF  
TYPHUS FEVER\*

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My reasons for submitting this paper, based on 41 cases of serologically confirmed typhus fever, are, firstly, the conspicuous absence of rash in every case of the series; secondly, the presence of the disease in a mildly endemic form throughout the year including the dry and hot summer months in the plains of the United Provinces of India, from where hitherto such cases have not been reported; thirdly, the close resemblance of the fever to that due to any acute upper respiratory tract infection of influenzal type, from which it was difficult to differentiate the condition until a constant symptom-complex was recognized; and fourthly, the frequent rise of the titre of the Weil-Felix reaction to diagnostic level after the fastigium was passed, sometimes reaching the peak titre only after deservescence.

The 41 cases, all among military personnel, fall naturally into two groups, the first 11 being seen in the hills, and the second 30 in the plains.

The first series seen in 1937-38 was found at Lansdowne, Garhwal District, in the United Provinces of India, a military cantonment 6,000 feet above sea-level, and belonging to the same range of hills as Kumaon from where Megaw (1917), Blewitt (1938) and other workers have described cases of tick and louse-borne typhus. The military population of Lansdowne consisted of 4 Indian infantry battalions with ancillary services such as transport, supplies and medical; and the civilian population totalled about 3,500, mostly Garhwalis. Bathing facilities for the civilians were practically non-existent. Ticks, lice and bed-bugs abounded in the place but not in the military living quarters. Platoons of troops often went out to the neighbouring hills for camping up to 8 days at a time.

The clinical features of the cases were remarkably uniform and are now described.

The onset was fairly sudden with only mild chill but with severe headache, sore throat, and marked malaise. The temperature rose quickly from 100°F. to 102°F. and simultaneously the face became flushed. In 48 hours, there was suffusion of the eyeballs, moderate enlargement of the tonsils, a generalized wet redness of the throat, and the spleen was just palpable. The patient usually took to bed by this time. Typical rigors, either during the onset or later, were not seen.

\* Based on a paper read at a conference of pathologists in the Middle East, at Cairo, on 5th March, 1943.

*Course.*—The fever reached a height of 103°F. to 105°F. in 3 or 4 days, which was maintained for 6 to 8 days; defervescence took place by lysis in 3 or 4 days, the total duration of the febrile period being 12 to 14 days. *Delirium* was not noticed in any of the cases but *insomnia* was present uniformly, although in varying degrees, during the height of fever. There was a passing *pneumonitis* (moist râles with impaired air entry) in 4 cases, and one patient had what appeared to be acute catarrhal *bronchitis*. This bronchial condition was quite mild and lasted from the 4th to the 11th day by which time lysis was in progress. *Meningeal* symptoms were absent. Vomiting was not seen in any of the cases, but during pyrexia there was tendency to slight constipation, which, however, did not call for any active treatment. Beyond slight febrile *albuminuria* in 6 cases, no urinary abnormality was detected. The *tongue* was coated with thick fur, sometimes white and sometimes brown, throughout the febrile period. The *tonsils* remained enlarged and slightly inflamed, and pain in the neck as a result was often complained of, and had to be treated. The throat condition improved with the onset of lysis. The *pulse* was slow in proportion to the temperature, and this often led to confusion with the enteric group of fevers, but the pulse was not of the easily compressible type generally associated with typhoid fever. The *leucocyte count* was generally normal or only slightly raised but never less than normal; the highest count was 9,800, with neutrophilic increase. This again helped to differentiate the condition from straightforward enteric fever.

A prominent and uniformly present feature of the illness was the *toxæmia*, first appearing on the 4th or 5th day and disappearing literally by crisis with the onset of the pyrexial lysis. This *toxæmia* was shown by a general blunting of intellectual functions, not explained by the degree of fever present in the cases; there was a stunned and vacant look in the eyes; unwillingness to hold even simple conversation was common; patients would take feeds willingly enough but would otherwise prefer not to be nursed. Restlessness was only rarely seen and then not to any marked degree. They would recognize persons but would encourage none. It was difficult to assess whether active cerebration was actually painful or cerebration was simply retarded because of the illness. *Subsultus tendinum* was absent. Exhaustion as seen at the crisis of classical lobar pneumonia or towards the end of the 2nd week of typhoid was absent; and the *toxæmia* of these cases could have been compared with the 'typhoid state' of typhoid fever but for the absence of exhaustion. This *toxæmia*, however, did not presage any complication, nor was it found to be of any serious prognostic import; so much so, that one came to look upon it merely as a normal feature of the disease, like the throat condition and the fever.

*Rash*, deliberately and diligently sought for, was absent throughout the series, though some of the patients were fair-complexioned. Of course rash is often absent in endemic typhus (Bush, 1936; Megaw, 1942).

A minor feature of illness was the vague muscular pain in 3 of the 11 cases; this was present from the onset and disappeared when *toxæmia* supervened.

The fever abated by rapid lysis in all cases, and all symptoms improved concurrently. There was no instance of hyperpyrexia.

*Complications.*—None was encountered. Convalescence was uneventful and rapid, return to work being allowed in 2 to 4 weeks from the date of discharge from hospital—which was usually after 5 weeks. Four of the cases were seen again in 1941 and they were healthy, taking part successfully in all the regimental programmes which then were rather intensive. The other 7 cases were also healthy, but it was not possible to examine them personally. The rapid and uneventful convalescence noted in the series may suggest a good prognosis. But such a facile conclusion should not be drawn. All the cases were young adults in the best of health, living under excellent sanitary conditions with a balanced dietary and exercise. They physically represented some of the healthiest Indians. Extremes of age, poverty and malnutrition, lack of proper sanitary and medical care may alter the prognosis. In civilian practice at Jhansi a case was seen in which pneumonia supervened causing death.

*Diagnosis.*—Malaria, the enteric group of fevers, tuberculosis, acute infections of the upper respiratory tract, measles, and influenza were excluded by appropriate tests and clinical examinations. Blood cultures, done on 4th and 8th days of the illness in nutrient broth and sodium taurocholate, were negative; agglutination tests were negative to typhoid, paratyphoid A, abortus and melitensis—using O emulsion obtained from the Central Research Laboratory at Kasauli. The ultimate diagnosis of the cases was based on the Weil-Felix reaction (see table I) and the symptom-complex consisting of (a) the peculiar *toxæmia* already described disappearing suddenly on onset of lysis, (b) the absence of post-*toxæmic* exhaustion so typically seen after the crisis of pneumonia and towards the end of the 2nd week in typhoid, and (c) the slow sthenic pulse, all occurring in association with the throat condition which was uniformly present.

Attention is drawn to an important observation made by others also, that the titre of agglutination often rose to a diagnostic level towards the end of the febrile period and sometimes continued so in convalescence.

A titre of 250 was considered diagnostic. Beveridge and Underhill (1936) described typical cases of typhus complete with rash in which the Weil-Felix titre did not go higher than 250. A titre below 250 was also taken as evidence of

TABLE I

Showing Weil-Felix reaction titre of Lansdowne cases—denominators of fractions used

Case number	DAY OF FEVER								
	4th			9th			13th or 14th		
	X2	X19	XK	X2	X19	XK	X2	X19	XK
1	25	50	125	25	25	250	25	25	250
2	0	25	50	25	0	125	0	0	125
3	25	25	125	0	0	125	25	0	500
4	50	50	125	25	25	250	25	50	250
5	0	25	50	25	0	250	25	0	125
6	0	0	50	25	0	125	0	0	125
7	25	0	50	25	0	125	0	0	250
8	0	0	0	0	0	50	25	0	125
9	25	0	50	0	25	50	0	0	250
10	25	25	50	25	0	50	25	50	500
11	0	0	50	0	25	125	0	0	125

typhus if it showed a gradual rise. In places such as England, a titre even as low as 100 has been recommended for diagnosis (Megaw, 1942), but such a low titre could not hold for places where the disease is endemic. The symptom-complex already described, the clinical similarity of the cases to those seen earlier in Malay, and

also to those described in the literature, and the uniformly positive agglutination reaction with XK lead to a diagnosis of typhus.

It will be noticed that all the cases showed the highest titre against XK and either *nil* or low agglutination against X2 and X19. This would bring the group in line with scrub typhus

TABLE II

Showing Weil-Felix reaction titre of Jhansi cases—denominators of fractions used

Case number	DAY OF FEVER																	
	4th			9th			15th			20th			25th			30th		
	X2	X19	XK	X2	X19	XK	X2	X19	XK	X2	X19	XK	X2	X19	XK	X2	X19	XK
1	0	0	50	0	25	50	0	0	125	0	25	250	25	0	125	Not done		
2	25	25	125	0	25	125	0	0	250	0	0	50	0	0	50	0	0	25
3	0	0	50	25	50	250	25	50	500	25	25	250	25	0	250	0	25	250
4	50	25	125	25	25	250	0	25	250	50	25	500	25	25	125	0	0	125
5	0	25	25	0	25	125	0	25	125	25	25	250	25	0	125	Not done		
6	25	25	50	50	25	50	25	0	250	0	0	125	0	25	125	0	0	125
7	25	50	125	50	25	125	0	25	125	0	0	250	0	0	125	Not done		
8	0	0	50	0	25	125	0	0	125	0	0	250	0	0	125	Not done		
9	25	50	50	25	25	125	25	0	125	0	0	125	0	0	50	0	0	50
10	0	0	50	0	50	125	0	25	250	0	0	50	0	0	125	0	0	50
11	50	0	25	25	0	25	25	25	125	0	0	125	0	0	250	0	0	50
12	0	0	50	25	50	250	25	0	250	0	0	125	0	25	50	Not done		
13	0	0	50	25	25	125	25	0	250	25	50	1,000	0	0	500	0	25	500
14	0	25	25	0	0	250	0	25	250	0	0	125	0	25	125	Not done		
15	0	25	50	25	50	50	0	50	500	0	50	500	0	50	250	0	50	250
16	50	50	125	25	50	125	25	50	250	50	0	125	0	0	125	Not done		
17	0	0	125	25	50	50	0	25	500	0	0	250	0	0	250	0	0	125
18	0	25	50	0	25	125	0	50	500	0	25	250	0	25	125	0	0	125
19	0	0	50	0	25	250	0	0	250	0	0	250	0	0	125	0	0	125
20	25	0	250	25	0	500	25	25	500	0	0	250	0	0	50	0	0	50
21	0	25	125	0	0	250	0	25	250	Not done			0	0	125	0	0	125
22	0	0	50	0	0	250	25	0	250	Not done			25	0	125	0	0	125
23	0	0	125	0	0	125	0	25	125	0	0	250	0	0	250	0	0	50
24	25	0	125	0	25	250	25	0	1,000	25	0	250	0	0	250	0	0	250
25	25	50	250	25	50	1,000	25	25	500	0	25	500	0	0	250	0	25	250
26	0	25	125	0	0	500	0	0	500	0	0	250	0	0	250	0	0	125
27	0	25	50	0	50	250	0	0	250	0	0	125	Not done			0	25	50
28	0	50	50	0	50	125	0	50	125	0	0	250	0	0	125	0	0	125
29	0	0	50	0	0	125	0	0	250	0	25	250	Not done			0	0	125
30	0	0	125	0	25	250	0	50	500	0	0	125	0	0	125	0	0	50

of Malay, cases of which are similar to the group described above, though in scrub typhus adenitis and sometimes ulcers due to the bite of the vector mite are seen (Lewthwaite and Savor, 1936). They also showed that scrub typhus was essentially a 'place disease'; the limitation of the cases of this series to the neighbourhood of Lansdowne would suggest that these too were instances of 'place disease'.

No vectors were found, but the disease was certainly not louse borne and probably not flea borne either. Ticks and mites are left as possible vectors, but further studies are required of this matter. It is suggested that, in view of only XK showing diagnostic agglutination, the vector was possibly a mite. It may be of interest to note that the vector of scrub typhus of Malay is a mite.

*Second series.*—The experience gained in the above cases enabled the collection of 30 cases at Jhansi, the Brigade Laboratory of which catered for 9 hospitals situated at Jhansi, Nowgong, Muttra and Agra—all places in the plains in the United Provinces of India or nearby. Summer temperature varied from 100°F. to 120°F. in the day and was 10°F. to 20°F. cooler at night; the winter temperature came down to 60°F. at places. Nineteen cases were seen at Jhansi, 8 were from outstations, and 3 were from the records of cases by the late Lieut.-Colonel H. S. Rajan, I.M.S., who commanded The Indian Military Hospital, Jhansi, from 1939 to 1942. Colonel Rajan had also independently observed such cases in Lucknow.

The clinical features of this series, being closely similar to those of the first, will not be described again. The absence of rash, the toxæmia, the uniformly similar pyrexial course, the throat condition, insomnia, occasional passing pneumonitis or bronchitis, slow sthenic pulse, and absence of leucopenia characterized this series also. There was no complication or death.

Systematic agglutination tests in this series were extended into the convalescent period and the results are given in table II.

No vector could actually be associated with any of the cases, but all the cases of this series would be exposed to bites by fleas, sand-flies, ticks, and mites during outdoor training, these insects being common around Jhansi; lice, however, were well under control and generally absent.

The observations already made about the rise of the agglutination titre apply to this series also—more so, for the agglutination tests were continued longer.

It should be mentioned here that a proteus bacillus was grown from the urine of case nos. 4, 11, 13 and 29. In each instance it was agglutinated by the homologous serum.

There can be no doubt about the diagnosis being typhus fever in these cases. Where the titre of agglutination is lower than 250, the diagnosis has to be accepted in view of the

gradual rise in titre and of the symptom-complex already referred to.

The seasonal incidence of the 30 cases is shown in table III:—

TABLE III

*Showing incidence of cases by temperature*

Month	Average day temperature	Number of cases
December ..	60°F.-90°F.	13
January ..		
February ..		
March ..	80°F.-100°F.	4
April ..		
May ..	100°F.-120°F.	6
June ..		
July ..		
August ..	85°F.-100°F.	2
September ..		
October ..	70°F.-95°F.	5
November ..		

It is clear that the majority of the cases occurred during the cooler months, but the six cases in the hot and dry months of April, May, and June would lead to a natural conclusion that while cooler seasons allowed typhus cases to occur more frequently, it was quite possible for cases to occur in the hot seasons also; in other words, the disease was present throughout the year.

*Discussion.*—Typhus fever in hot weather is not common, but dried lice have remained infective for 3 months (Starzyk, 1938) and dried faeces of infected lice have retained their virulence for 12 months (Blanc and Baltazard, 1938). Such experimental evidence is in accordance with the occurrence of these 6 cases in the summer.

The frequent late rise of the Weil-Felix reaction titre brings the question of diagnosis into prominence. Unless agglutination reactions are carried out serially, and are extended far into the convalescent period, cases may be missed. This may not make any difference to the particular case, but the possibility of an outbreak occurring should not be forgotten. It is true that zootic typhus does not generally produce a louse-borne human epidemic, but at least one epidemic among human beings caused by flea-borne typhus has been recorded from Palestine (Kliger and Comaroff, 1936). If those infected in such an epidemic were also immediately afterwards exposed to louse infestation, the possibility of the lice then becoming infected and starting a human epidemic cannot be overlooked.

#### Summary

1. Two series of typhus cases are described.
2. A uniform symptom-complex sufficient to diagnose the disease on clinical grounds alone has been crystallized.

(Continued at foot of next page)



# COMPLEMENT-FIXATION TESTS PERFORMED BY N. H. TOPPING, U.S. PUBLIC HEALTH SERVICE,\* AND OTHER OBSERVATIONS IN 'MYSORE TYPHUS'

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and

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In previous publications (Heilig and Naidu, 1941, 1942, 1942a) the experiences on fourteen cases of typhus have been reported, covering the period from November 1940 up to February 1942. In the following twelve months, another eighteen cases came under our observation.

A brief survey of the epidemiological, clinical and serological facts, observed in these thirty-two cases from November 1940 to end of February 1943, is presented in this paper.

*Seasonal incidence.*—January, three; February, three; March to July no case, except for one quite atypical case (no. 16) which was admitted on 1st June, 1942, and will be described in some detail. August, six; September, two; October, three; November, six; December, eight.

*Geographically.*—Twenty-two cases came from Mysore city, ten from large villages up to 40

miles from Mysore, and one case came from a distance of about 75 miles. The occurrence of two cases in one family was only seen once (Heilig and Naidu, 1942).

*Age.*—Three to sixty years.

*Sex distribution.*—Twenty-four males, eight females. The proportion of male to female hospital beds is about two to one.

*Community.*—Twenty-seven Hindus, five Muslims, the latter forming almost one-third of all our hospital patients.

The clinical picture did not differ in any essential point from our previous description (Heilig and Naidu, *loc. cit.*). *Fever* lasted between ten and twenty-two days with an average duration of seventeen days. Some patients stated that it started with a rigor; this was not reported in the previous seasons. The *respiratory system* remained free from complications. *Conjunctivitis* was present in most of the cases, but definitely absent in three of them. The *rash*, which was distinctly visible in all these cases, appeared between the fourth and tenth, usually on the sixth or seventh day; it was most abundantly developed on back and extremities, regularly including wrists and ankles. A considerable involvement of the face, such as is seen in the photo of case 18 (see plate VI), was rarely found. The maculo-papular efflorescences of dark purplish or copper colour left dark-stained spots for weeks or months afterwards. Peeling was seen occasionally. A *leucocytosis* of 12,000 to 20,000 was a constant feature.

During the last season, the *Weil-Felix* reaction was found positive in a much higher percentage of cases and, in some of them, reached higher titres than before because (since November 1942) in in-patients the test was repeated every two days.

Table I shows the results obtained during the last season.

It is noteworthy that all the three *Proteus* strains are agglutinated in practically every case, that the titres vary quickly and that sometimes the agglutinins are present only for a short time.

The *Neill-Mooser* reaction was positive in four (nos. 4, 16, 22 and 25), negative in twelve cases. Guinea-pigs, inoculated with the blood of case nos. 22 and 25, have been sent to Lieut.-Colonel S. S. Sokhey, Haffkine Institute (Bombay), where Dr. S. R. Savor had for the past eight months maintained in guinea-pig passages one of the *Rickettsia* strains; the other one died out after several passages.

*Wassermann*—(or Kahn or Kline) reactions were positive in six cases; they became negative during the convalescence in five of them.

One exceptional case (M. R., Brahmin male, aged 40), a temple servant, came from a village, about 20 miles from Mysore. Admitted on 1st June, 1942, the 11th day of illness, in a comatose condition, he showed a remittent fever which varied between 100°F. and 102°F.; he became afebrile on the 16th day, one day prior to his death, which occurred due to peripheral circulatory failure. His eyes had a 'blood shot'

(Continued from previous page)

3. The disease can occur in dry and hot weather.

4. The rise in agglutination late in the course of the illness is emphasized, and a plea is made for continuing the Weil-Felix reaction far into the convalescence.

5. The possibility of such endemic cases giving rise to a louse-borne human epidemic is mentioned.

Thanks are due to Jemadar P. N. Mehra, I.M.D., for help with laboratory investigations; to Captain M. Sanjiva Rao, I.M.S., for help in preparing this paper, and to the late Lieut.-Colonel H. S. Rajan, I.M.S., for records of his 3 cases and advice; had Colonel Rajan been living to-day this paper would have been written jointly.

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TABLE I

Case number	Designation, age, month of occurrence	Duration of fever	Day of rash appearance	WEIL-FELIX REACTION				REMARKS
				Day of disease	OX19	OXK	OX2	
15	Hindu boy, 14, February 1942.	17	4	18	Neg.	Neg.	Neg.	Admitted on 15th day.
16	Brahmin male, 40, June.	14	2	11 13	1:1,280 1:20,000	Neg. Neg.	Neg. Neg.	Exceptional case. Died on 16th day. Neill-Mooser reaction positive. Mild case.
17	Brahmin boy, 12, August.	12	5	14 19	Neg. Neg.	Neg. 1:80	Neg. 1:160	
18	Brahmin lady, 45, August.	21	7	10 15	Neg. 1:20	Neg. 1:40	Neg. 1:80	Diabetes. See photo (plate VI). Neill-Mooser reaction negative. Out-patient.
19	Brahmin male, 30, October.	18	7	20	Neg.	1:20	1:80	
20	Brahmin boy, 14, October.	16	7	16	1:20	1:40	1:80	Out-patient. Neill-Mooser reaction negative.
21	Hindu male, 50, November.	22	?	14 18 24 26	1:20 1:80 1:40 1:40	Neg. 1:20 1:40 1:20	1:20 1:20 1:320 1:80	Neill-Mooser reaction negative.
22	Hindu male, 26, November.	15	9	11 13 15 18 22	1:40 1:40 1:80 1:160 Neg.	1:40 1:40 1:20 1:80 Neg.	1:80 1:40 1:20 1:80 Neg.	Neill-Mooser reaction positive.
23	Hindu boy, 14, December.	19	7	10	1:40	1:20	1:80	Out-patient.
24	Hindu male, 30, December.	19	8	9	1:40	1:40	1:320	Out-patient.
25	Muslim male, 20, December.	18	4	5 9 11 13 17 19	Neg. Neg. Neg. 1:20 1:40 1:40	Neg. 1:20 1:40 1:20 1:40 1:20	Neg. 1:40 1:40 1:20 1:80	Compl.-fix. test see table 2. Neill-Mooser reaction positive.
26	Brahmin male, 20, December.	15	7	9 11 13 15 17 19	1:80 1:80 1:40 1:40 1:80 1:40	1:320 1:160 1:40 1:40 1:40 1:20	1:40 1:40 1:40 (80) 1:80 (160) 1:80	Compl.-fix. test see table 2. Neill-Mooser reaction negative.
27	Brahmin male, 30, December.	12	7-8	10 12 14 20	1:40 1:40 1:40 1:40	1:40 1:40 1:40 1:20	1:80 1:160 (320) 1:160 (320) 1:40	Compl.-fix. test see table 2. Neill-Mooser reaction negative.
28	Hindu male, 35, January.	18	10?	12 14 16 20	1:20 1:40 1:40 Neg.	1:80 1:160 1:40 Neg.	1:160 1:160 (320) 1:80 1:80	Neill-Mooser reaction negative.
29	Muslim female, 50, January.	18?	5?	5? 7 9 11 13 15 17 19 22	1:320 1:320 1:320 1:320 1:160 1:160 1:160 1:160 1:80	1:160 1:80 1:80 1:80 1:40 1:40 1:40 Neg. 1:40	1:80 (160) 1:40 1:40 1:40 Neg. 1:80 1:80	
30	Hindu male, 19, February 1943.	17	6	10 12 14 16	1:40 1:80 1:80 1:80	1:40 1:20 1:40 1:40	1:40 1:40 1:80	
31	Muslim male, 55, December.	17	4	5	Neg.	Neg.	Neg.	Out-patient.
32	Brahmin male, 26, November.	15	5	13 7	Neg. 1:40	Neg. 1:80	1:80 1:80	L.M.P. out-patient.

appearance. The rash was faintly visible on the dark skin; it was confined to shoulders and upper arms and almost disappeared a day or two before he expired. There were no respiratory complications. Leucocyte count 7,400. Cerebro-spinal fluid: protein content increased, cells 6 per c.mm. The *Weil-Felix* reaction on the 11th day showed a titre of 1:1,280 for OX19; on the 13th day it shot up to 1:20,000; no agglutinins for OXK or OX2 were present. No lice or mites were found on him, and he had nothing to do with cattle, whereas plenty of rats were present in the temple compound.

The peculiarities of this case are that it occurred in May to June (off the local season), that it ended fatally, showed no leucocytosis, that OX19 was agglutinated with an exceptionally high titre and that no co-agglutination was found.

Every known vector type (louse, flea, tick and mite) of rickettsioses has been reported from

the test was negative in all their cases of Rocky Mountain spotted fever. Plotz and Wertman (1942), working with antigen from Rocky Mountain spotted fever, found complement fixation positive in all their (nine) cases of this disease and consistently negative in Brill's disease.

We obtained sera of case nos. 25, 26 and 27 under strictly aseptic conditions, filled them in sterile ampoules and despatched them by air mail (10th January, 1943). One month later, Dr. Topping had carried out the complement-fixation tests (in Bethesda, Md., U.S.A.), using as antigen the specific virus of epidemic typhus, American endemic typhus and Rocky Mountain spotted fever, grown in the yolk sac of fertile eggs (Cox, 1938). His results are given in table II.

TABLE II

*Showing the results obtained and communicated by Dr. N. H. Topping*

	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512	Day of disease
Patient 1 (case no. 25)									
Rocky Mountain spotted fever.	4+	4+	4+	4+	2+	1+	Trace	0	25
Epidemic typhus ..	1+	Trace	0	0	0	0	0	0	..
Endemic typhus ..	2+	1+	0	0	0	0	0	0	..
Patient 2 (case no. 26)									
Rocky Mountain spotted fever.	4+	4+	4+	4+	4+	4+	4+	2+	21
Epidemic typhus ..	1+	Trace	0	0	0	0	0	0	..
Endemic typhus ..	4-	4-	4-	3+	2+	1+	1+	0	..
Patient 3 (case no. 27)									
Rocky Mountain spotted fever.	4+	4+	4+	4+	4+	4+	4+	1-	20
Epidemic typhus ..	4+	4-	1+	0	0	0	0	0	..
Endemic typhus ..	4+	4-	4-	1+	1-	0	0	0	..

various parts of India, although clinical evidence exists only for lice and ticks.\* We were unable to establish rat fleas or cattle ticks as the vector of our cases, lice and mites being excluded on clinical and serological grounds.

Our attempts towards determining the proper place of the Mysore type in the system of rickettsial diseases found an unexpected powerful support from the U.S. Public Health Service. N. H. Topping, having read our previous reports, requested us to send him sera of our cases for carrying out complement-fixation tests.

The complement-fixation test in rickettsioses was introduced by Castaneda (1936) for the differentiation of Mexican typhus from Brill's disease. It found its most important application when Bengtson and Topping (1942) discovered that an antigen from endemic typhus causes complement fixation in all (53) cases of laboratory infection with endemic typhus, becoming positive on the tenth day and remaining so for five and a half years, whereas, using the same antigen,

We reproduce in full the comment of the results, given by Dr. Topping in his personal communication (2nd February, 1943). 'These results indicate to us that the sera of these three cases show antibodies more nearly similar to those seen in Rocky Mountain spotted fever than in those cases of ours of endemic typhus. It would seem to indicate further that the disease which you consider to be endemic typhus in Mysore is caused by a virus which produces antibody that fixes complement to a higher titre with a rickettsial antigen from Rocky Mountain spotted fever than it does with a rickettsial antigen prepared from either endemic or epidemic typhus. The fact that there is some cross fixation with endemic typhus is very interesting and is unexplained. We have seen cases of so-called Rocky Mountain spotted fever here in this country, the sera of which produced some cross fixation with endemic typhus, but where the titre with Rocky Mountain spotted fever is much higher as it is in your cases. We have also seen some cases of endemic typhus that crossed in the complement-fixation test with Rocky Mountain spotted fever also, but where

\* There is now clinical evidence of flea- and mite-borne typhus.—Editor.

the titre was consistently higher against endemic typhus antigen.'

We previously pointed out (Heilig and Naidu, 1942) the clinical and serological identity between our cases and the X2-typhus of Boyd (1935), which certainly is not a louse-, mite- or rat flea-typhus. By exclusion we inferred that the Mysore group belongs to the 'undetermined type' which, apart from Boyd's X2-typhus, includes Rocky Mountain spotted fever, San Paolo typhus, fièvre boutonneuse and Kenya typhus. All these forms, characterized by a distribution of the rash similar to that seen in our cases, and by the presence of agglutinins for all the three *Proteus* strains (OX19, OXK, OX2), are transmitted by ticks. Only for the cases reported by Boyd and ourselves, the vector is not established, although we tried to trace it, inoculating guinea-pigs with emulsified rat fleas and cattle ticks (Heilig and Naidu, 1942). However, on clinical evidence, we tentatively classified the Mysore type as *tick typhus* (Heilig and Naidu, 1942a).

Topping's application of the complement-fixation test to three of our cases corroborates our previous conclusions and contributes considerably towards the solution of the classification and vector problems of Indian typhus. It shows that those cases seen in India which clinically resemble cases of the Mysore type are closer related to the spotted fever group than to any other form of rickettsial diseases.

The Mysore type may resemble one form of the spotted fever group more than others; it seems to show the closest similarity with the eastern type of Rocky Mountain spotted fever, in the duration of fever, the distribution and appearance of the rash which regularly involves ankles and wrists, the good prognosis, the mild and inconstant Neill-Mooser reaction in guinea-pigs and the serological behaviour. Even the unusual cross fixation with endemic typhus finds its counterpart in the observation (Reimann, Ulrich and Fisher, 1932) that the Minnesota variant 'seemed to represent a transitional type between spotted fever and murine typhus', although recently opinion has been that it is a very mild form of spotted fever (Zinsser and Bayne-Jones, 1939). On these grounds, it may be permissible to surmise that further search for the Mysore vector has to follow the lines which proved successful in the eastern type of Rocky Mountain spotted fever. Dyer (1935) and co-workers established that the dog tick (*Dermacentor variabilis*) transmits this disease and that dogs are the reservoir for the virus. In India, Napier was the first to draw attention to dogs as carriers of rickettsiae (Editorial, 1936). For further investigations it should be kept in mind that in the U.S.A. not only the indigenous *Dermacentor variabilis* but also, according to Parker and Davis (1933), the European dog tick, *Rhipicephalus sanguineus*, the vector of fièvre boutonneuse, is capable of transmitting the virus.

### Conclusion

Topping's findings that three cases of so-called Mysore typhus gave complement-fixation tests predominantly positive for Rocky Mountain spotted fever, with a cross fixation for endemic American typhus in two of them, make it most probable that the local type is closely related to the spotted fever group. Such a conception conforms well to the clinical syndrome and the results of the Weil-Felix reaction in our cases. Ticks being the vectors of the rickettsiae in all the various types of spotted fever, cattle ticks having been unsuccessfully tested in some of our cases, and, none of the patients seen here having had any obvious contact with jungle ticks, dog ticks are probably the local vector.

### Summary

Thirty-two cases of so-called Mysore typhus have been diagnosed from November 1940 to February 1943.

Topping performed complement-fixation tests in three of these cases with antigen from Rocky Mountain spotted fever, endemic American and epidemic typhus. His results are reported and correlated with our clinical and serological findings.

The vector question is discussed with special regard to Topping's findings.

We have great pleasure in expressing our sincere thanks to Dr. N. H. Topping for his request to send sera of our cases to him, for performing with them complement-fixation tests and for his kind permission to report his results. Our thanks are also due to the local practitioners whose co-operation enabled us to include in this report several cases under their treatment.

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## A METHOD OF RAPID STAINING OF INTESTINAL FLAGELLATES

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It is recognized that the staining of flagella of flagellate protozoa is often no easy task. Fresh faecal samples containing flagellates can be subjected to treatment with Donaldson's eosin-iodine solution in order to demonstrate the flagella, but such a preparation is not of a permanent nature. Wet fixed films of flagellates can be stained with Heidenhain's iron-alum hæmatoxylin, but in this method too, one often experiences great difficulty in bringing about the proper differentiation of the different organelles and at the same time maintaining a proper depth of staining for the flagella. This is particularly so in the case of very minute flagellates.

Shortt (1923) fixed wet films of flagellates by exposing the film to the vapour of 4 per cent osmic acid solution and subsequently stained the dry film with Giemsa after the manner of blood films. This method produces excellent results, and the flagellates, however minute, stand out very clearly. This method, however, involves the use of an expensive material, viz, osmic acid. Noller's method, as quoted by Stitt *et al.* (1938), involves the use of a fixative and, after washing with water and saline, the film has to be immersed in clear sterile serum (e.g., that of the horse) for 5 to 10 minutes and then fixed again in absolute alcohol before staining according to the blood film technique. This method takes time and, in addition, it is difficult to ensure that sterile serum shall be always ready to hand.

This article describes a process of staining which does not involve the use of an expensive reagent, but which produces excellent results. In less than half an hour the preparation is ready for microscopical examination. By this method one is able to count quickly the number of flagella, to see the disposition of the different organelles, and to ascertain the systematic position of the organism. The photomicrographs (see figures 1 to 12, plate V) illustrating this article are taken from preparations stained by the method described below.

### Technique

With a long fine-bore pipette, remove the material (faecal or culture) containing the flagellates, place it on a very small drop of dried mammalian blood\* on a slide, allow the material to mix with the blood, and then draw it back into the same pipette. The sucked-up fluid should have a blood red colour; if it has not, the material may be pipetted back to another droplet of dried blood, and the process should

(Concluded at foot of next column)

\* A worker's own blood can be used with great advantage. Prick the finger-tip with a sharp needle. Then press the bleeding finger on a clean slide so as to have several impressions of the blood on the same slide. Cover the slide and allow it to dry. This dried blood can be stored in some dry dust-proof place and can be used for a week or ten days without any appreciable change in the requisite reaction.

## PROTEIN HYDROLYSATES AS TRANS- FUSION MATERIAL

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DUE to the increasing demand for large quantities of transfusion material for combating shock and hypoproteinæmia, and due to the high cost and other difficulties associated with the

(Continued from previous column)

be repeated. Now take a clean grease-free slide, warm it gently over a flame, and, with gentle pressure on the teat of the pipette, squeeze out the contents in long streaks on the slide. Only a small amount of the fluid should come out of the pipette at one time, so that the material dries up immediately it comes in contact with slide. With a little practice, a steady flow can be maintained so as to give parallel edges to the streaks. To accelerate the process of drying, the slide may be kept exposed to a gentle breeze from a table fan while the operation is being carried out. In this case, warming of the slide is not necessary. Stain the slide with either Leishman or Giemsa.

A thin film of this material can also be made after the manner of a blood film and stained as above. In such a preparation, the flagellates are always found at the 'fish-tail' end of the film. The writer, however, is of the opinion that the fine streak method described above is more convenient for rapid examination than the thin film method. Moreover, in the thin film method, the flagellates are slightly distorted, since they are dragged in the process in making the film; while in the streak method the organisms are allowed to flow on to the side in a steady stream and are allowed to dry immediately. This precludes any chance of distortion. Flagella stained by this method, however, appear thicker than normal owing to the flattening that takes place during drying.

This method, though unsuitable for detailed cytological studies, is, nevertheless, a great aid to the proper understanding of the morphology of the organism. The flagella of the non-parasitic flagellates can also be stained by this method with great ease.

In conclusion I should like to place on record my indebtedness to my teacher, Rai Bahadur Dr. G. C. Chatterjee, who about twenty years ago initiated me into this method of staining intestinal flagellates, which I propose to designate 'Chatterjee's method'.

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Fig. 1.



Fig. 2.



Fig. 3.

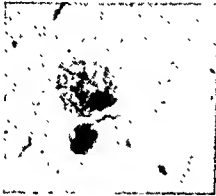


Fig. 4.

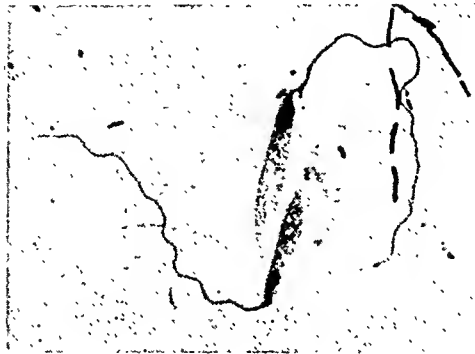


Fig. 5.

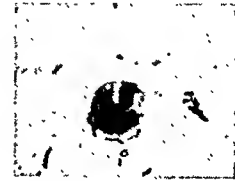


Fig. 6.

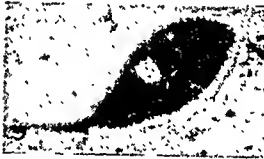


Fig. 7.



Fig. 8.

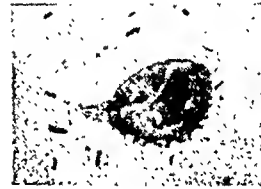


Fig. 9.



Fig. 10.



Fig. 11.

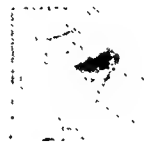


Fig. 12.

#### EXPLANATION OF PLATE V

Fig. 1.—Trichomonas from the caecum of porcupine. Note the posterior axostylar chromatic ring.

Fig. 2.—Trichomonas from the caecum of porcupine. Note the basal fibre and the rhizoplast.

Fig. 3.—Trichomonas from the caecum of porcupine. Note the clear cytoplasm and the typical disposition of the nucleus.

(N.B.—In this trichomonas all the three free flagella were found to be directed posteriorly.)

Fig. 4.—Retortamonas from the caecum of guinea-pigs.

Fig. 5.—Prowazekella from the gut of a lizard.

Fig. 6.—Hexamastix from the gut of a lizard.

Fig. 7.—Chilomastix from the rectum of a Himalayan toad.

Fig. 8.—Trichomonas from the intestine of a Himalayan lizard.

Fig. 9.—Trichomonas from the rectum of a Himalayan frog.

Figs. 10 and 12.—Pentatrichomonas from the gut of a Himalayan crow.

Fig. 11.—Retortamonas from the mid-gut of a cockroach.

(Photographs were taken with Spencer's vertical camera and incandescent lamp. Magnification  $\times 715$ .)





PROTEIN HYDROLYSATES AS TRANSFUSION MATERIAL : E. K. NARAYANAN AND K. V. KRISHNAN. PAGE 158

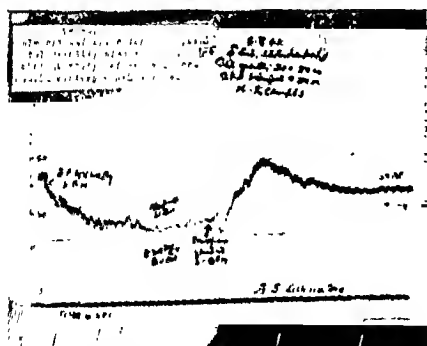


Fig. 1.



Kymograph picture of serum transfusion in cat for comparison.

preparation of human plasma and serum for the purpose, various other cheaper and more easily prepared substitutes are being tried. One such is protein hydrolysates. Elman and Lischer (1943) have shown that 'in fatal surgical shock experimentally produced by repeated hæmorrhage, immediate replacement with a solution of hydrolysed protein containing amino-acids and polypeptides exerted a definite therapeutic effect as shown by prolongation of the survival time, and increase in the amount of hæmorrhage which could be sustained and a higher level of blood pressure as compared with the controls in which dextrose alone was used or in which there was no replacement'. When this publication appeared, we were already engaged in preparing protein hydrolysates for bacteriological purposes, we immediately intensified our efforts and attempted to make a product suitable for transfusion purposes. Success was achieved with a papain digest of meat. The present communication gives a brief account of the method of preparation and the results obtained in experimental animals and in man.

#### Method

The method recommended by Krishnan and Narayanan (1941) for hydrolysing proteins for bacterial nutrition was used with certain modifications. The papain digestion of meat was conducted at 50°C. for 24 hours and the filtrate made suitable for intravenous injection by removal of undigested proteins and meta-proteins (anaphylactogens) by repeated heat coagulation. To the standardized final filtrate, glucose and sodium chloride were added to yield a mixture containing 5 per cent protein hydrolysates, 5 per cent glucose and 0.85 per cent sodium chloride, and the mixture was finally sterilized in transfusion bottles.

#### Results

So far, 40 different batches have been prepared and tested on cats in a state of experimentally induced hæmorrhagic shock according to the technique of Krishnan, Mukherjee and Dutta (1944). In all of them the type of result obtained was exactly the same as shown in figure 1 (see plate VI), which is a photograph of the kymograph picture. It will be seen that, on transfusion with the protein hydrolysate mixture, there was no reaction (fall of blood pressure or respiratory distress), the rise in blood pressure was steady though not very high, and was well maintained for 3 hours—the period of the experiment. The report on the quality of this product by the Biochemical Standardization Laboratories (Dr. B. Mukherjee and Dr. N. K. Dutta, who very kindly conducted the cat experiments for us) is that it is safe for transfusion and that its value in the treatment of shock would probably come midway between that of serum and glucose saline. On receiving this report the product was administered to advanced inanition cases and the results

were very satisfactory. So far, 106\* cases have been treated, and the beneficial effects noted have led us to present the results in a separate communication (Krishnan, Narayanan and Sankaran, 1944). In this article the results obtained in the laboratory animals are alone discussed.

#### Discussion

The results recorded above show that hydrolysed proteins can safely be administered to cats (40 to 80 c.cm.) without any adverse reaction. The results however give this product a place lower than serum or plasma and higher than glucose saline in the treatment of shock. The reasons for this probably are two. Firstly, the amino-acids and peptides contained in the mixture take time to be converted into serum proteins. Elman and Weiner (1939) have pointed out that usually 3 to 6 hours elapse before an appreciable rise in the serum-protein level can be noted. The few tests conducted on the protein level of the sera of cats before and after transfusion in our experiments also confirm these findings. We are therefore led to presume that the immediate benefit from this transfusion is due chiefly to the glucose saline administered rather than to the protein hydrolysate present. The real benefit arising out of the increase in serum proteins which invariably follows the administration of protein hydrolysate takes time (a few hours) to appear. When this happens, the temporary benefit conferred by glucose saline in the product is continued and maintained for a longer period, due to the hydrolysates producing a rise in serum proteins. This fact may have to be considered in the selection of cases for this therapy. All cases of traumatic shock may not equally benefit by this treatment. While the less urgent cases may benefit by it as much as with serum, the more urgent cases may not show the same degree of improvement.

Secondly, the amino-acid mixture cannot be given too rapidly or in too large quantities. The experience with our product so far shows that administration at a rate over 4 c.cm. per minute may not be well tolerated, and that it may not be advisable to give more than a pint of our product at a time to man. Serum, on the other hand, has been administered in much larger quantities and in shorter periods in certain types of emergencies without any ill effects.

#### Conclusion

While our product has a definite value in the treatment of chronic hypoproteinæmic conditions such as starvation, it is not superior to serum or plasma in the treatment of traumatic shock. Unless it is further reinforced with suitable colloids to bring the blood pressure raising quality to the level of serum, it can occupy only a second place in the treatment of acute traumatic shock. Experiments are in progress to prepare a product which will not only be

(Concluded on next page)

\* The number of cases treated is now much greater.

## PROTEIN HYDROLYSATES IN THE TREATMENT OF INANITION

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and

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### Introduction

WITH the prevalence of famine conditions in Bengal this year, starving destitutes from rural areas came to Calcutta in large numbers in search of food and work. Those that were unsuccessful in their quest made the open streets their home, and many of these in course of time reached the stage of advanced inanition. Arrangements had to be made to pick them up from the streets and send them to emergency hospitals for treatment and care. It was found that about 25 per cent of the cases removed to hospitals were in an almost moribund state. They were unable to take even liquids by mouth, and the death rate among them was very high. The immediate problem confronting the doctors in the emergency hospitals was to revive these collapsed cases by some suitable parenteral therapy and thereby prevent the high mortality. Intravenous injections of glucose saline were first tried and although improvement in the general condition was noted in most cases it was not sometimes sustained or uniform and the death rate was not markedly reduced. The administration of normal human serum was next tried in a few cases with

some benefit. Yet the clinicians felt that there was urgent need for some better transfusion material, if the advanced starvation cases were to be saved from death. Being already engaged in the investigation of various transfusion materials used for combating shock including protein hydrolysates, it struck us that a mixture of protein hydrolysates, glucose and vitamins would, on theoretical grounds, be an ideal fluid for parenteral administration to cases of inanition. We had on hand a number of samples of hydrolysates prepared by us in our laboratory and one of these had been proved to be satisfactory for transfusion purposes by laboratory tests on animals (Narayanan and Krishnan, 1944). It was decided to try this product immediately on humans, and a case of inanition collapse was treated with it on 8th November, 1943. Since then many injections have been given and results were very encouraging. In this preliminary note we are presenting a brief account of this therapy.

### Historical

Henrique and Andersen (1913) were the first to show that hydrolyzed proteins could be safely given intravenously to protein-starved animals, and that they supported life and growth, and maintained the animals in nitrogen equilibrium. Elman (1942) and Elman and Lischer (1943) found that solutions of amino-acids and peptides can be administered intravenously to man in fair amounts without any very serious reactions, and that patients suffering from cancer and ulceration of the intestinal tract and after surgical operations could be maintained in nitrogen equilibrium by their use. These findings stimulated us to prepare protein hydrolysates in different ways and in a form better suited for intravenous administration. This investigation was commenced in the early part of 1943.

*Methods of preparation known.*—Protein hydrolysates have been prepared by previous workers in one of two ways: (1) Acid hydrolysis and (2) Enzyme hydrolysis.

*Acid hydrolysis* is the easier method as it presents no great technical difficulties. But in this method at least one essential amino-acid (tryptophane) is known to be destroyed by the hot acid, and has to be separately prepared and added to the hydrolyzed mixture in order to make it efficacious. This extra step makes the product expensive. The delay and difficulty involved in obtaining pure tryptophane in sufficient quantities discouraged us from attempting this method of preparation in the present emergency. Acid hydrolysates have been used by Elman and others and their reports show that they are fairly satisfactory, though not absolutely safe in all cases.

*Enzyme hydrolysis* is also not a difficult method. It is quick and cheap. But in this method the hydrolysis is generally incomplete and the mixture may contain, in addition to

(Continued from previous page)

cheap and easy to make but will also be as good as serum with regard to its osmotic properties. Should these experiments prove successful then the cost of treatment of traumatic shock with such a product will be only a fraction of that by whole blood, plasma or serum.

### Acknowledgment

Our thanks are due to Dr. J. B. Grant, Director, All-India Institute of Hygiene and Public Health, for constant encouragement and help; to Dr. B. Mukherjee, Director, Biochemical Standardization Laboratories, for testing our product and certifying its non-toxicity.

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amino-acids and simple peptides, higher polypeptides derived from the substrate as well as the enzyme. The latter have to be removed if they are found to be responsible for any allergic or other reactions. Elman (Mueller *et al.*, 1943) seems to have tried hydrolysis with trypsin. While his products gave fairly satisfactory results in a number of cases, in some they induced allergic and other reactions. We also found that the tryptic hydrolysates prepared by us invariably gave rise to toxic reactions in experimental animals. Although the degree of hydrolysis effected by trypsin is extensive, we felt that in view of the above finding it would be necessary to use other enzymes that would not give rise to toxic products. Success was achieved by the use of papain (*vide infra*).

*Mixtures of the ten essential amino-acids* separately prepared have also been used by some workers (Madden and others, 1943). While somewhat encouraging results have been obtained by some, others are of the opinion that pure amino-acid mixtures are not quite as good therapeutically as hydrolysate mixtures. The latter finding gains support from the view that in a patient with a negative nitrogen balance, a supply of essential amino-acids alone does not fully meet the need. Moreover, the preparation of pure amino-acid mixtures is time-consuming and expensive, and it may be a long time before they are made available in suitable amounts at a reasonable cost.

#### *Choice of ferment and substrate*

From a careful study of the methods of preparation described above, we came to the conclusion that a properly-prepared enzymic hydrolysate would be the cheapest and best product for parenteral therapy in this emergency. Pancreas trypsin which had mostly been used by previous workers, in our opinion, has two drawbacks. Firstly, the optimum temperature of its action being 37°C., it would be very difficult to avoid bacterial contamination and growth during digestion. This may be a possible explanation for the toxicity of some of the products. Secondly, despite all care in the collection and use of pancreas trypsin, there is always the risk of the presence of histamine or histamine-producing enzymes. In order to overcome these two drawbacks, a ferment capable of acting at higher temperatures and free from histamine and histamine-producing agents would be desirable. Although trypsin may act at higher temperatures, the degree of hydrolysis will be less extensive and the product will still be unsuitable for parenteral use due to the second drawback.

The vegetable proteolytic enzyme *papain*, which is readily available in large quantities at a low cost, answered the requirements, and was used. Its optimum temperature of action is 50°C. and its reaction products have been found to be free from histamine. While it is true that

the hydrolysis produced by papain is not quite so extensive as that produced by trypsin, this does not appear to be a handicap from the immunological and therapeutic points of view. Having selected papain, the choice of the substrate necessarily fell on meat proteins, as its action on casein and vegetable proteins is more limited.

#### *Our method of preparation*

The protein hydrolysate that is at present being made in the Institute is a papain digest of meat (*vide* Narayanan and Krishnan, 1941). The digestion is conducted at 50°C. for 24 hours. The extent of digestion is then tested by determination of formol titre, total solids and total nitrogen. A fractional analysis of the product is also made. The values obtained are used as guides for standardization of the product. The undigested proteins and meta-proteins which are usually small in amount and which are likely to provoke allergic reactions are removed by repeated heat coagulation at pH7. During the process of preparation, bacterial contamination is avoided through the use of an aseptic technique and a preservative (toluol). The final product is mixed with glucose and sodium chloride so as to give a mixture containing 5 per cent protein hydrolysate, 5 per cent glucose and 0.85 per cent sodium chloride. The mixture is then sterilized and tested before issue, biologically on cats for toxicity, bacteriologically for sterility, and immunologically for allergic reaction.

Analysis of the mixture has incidentally revealed that it contains riboflavine, nicotinic acid and thiamin. The vitamins in the mixture are of additional value in increasing the therapeutic efficiency in promoting glucose utilization, particularly in vitamin-starved individuals such as the destitutes in Calcutta.

#### *Rationale of therapy in inanition*

Just as glucose is administered intravenously as a means of supplying predigested carbohydrates, so hydrolyzed proteins are injected for supplying the nitrogen needs of a patient. In cases of starvation, the nitrogen need is more urgent than in the normal subject. In the former, where body proteins are being rapidly broken down, it is absolutely essential to administer proteins to save life. Even if sufficient glucose is given to meet the calorie needs, protein break-down will not be completely stopped and continued life may not be rendered possible.

Protein food may be administered by mouth, but it will need to be digested and absorbed by the gastro-intestinal tract. In advanced cases of starvation, because of impairment of digestive function, this is often not possible; the only other alternative then is to administer hydrolyzed proteins parenterally. If this is done and if, along with it, glucose and vitamin-B complex are administered, the starving tissues will receive the more important requirements in a form ready for utilization. Both on theoretical grounds and

from the experience so far gained, it seems justifiable to state that administration of glucose protein hydrolysate in suitable amounts will not only prevent depletion of essential body and plasma proteins but will also help in the synthesis of these and in the restoration of the patients to normal condition.

Here two questions may be asked: (1) why not give these hydrolysates orally, and (2) why not give serum or plasma intravenously instead of the protein hydrolysate? The answer to the first question is that protein hydrolysates can be given orally, but in patients with advanced inanition and collapse, absorption is slow and doubtful, and for quick effect parenteral administration is probably necessary. Also, after absorption from the intestine, the amino-acids first reach the liver and later only the tissues. If the liver is damaged, no synthesis will take place and also there will be delay in reaching the tissues which need them badly. Hence for the very advanced cases, intravenous injection is the method of choice. However, in children and in those cases where parenteral administration is difficult, oral or rectal administration of glucose protein hydrolysate may be resorted to with benefit. In the emergency children's hospital these methods have been found useful.

To the second question the answer is that tissue proteins and serum proteins are not directly interchangeable. The latter have to be autolyzed, and the amino-acids made available for synthesis. In advanced cases of starvation where there is dehydration, the need for tissue proteins is more urgent than the need for serum proteins which may be apparently normal due to the hæmoconcentration. Thus if serum is given, its utilization will depend upon the proper functioning of the enzyme systems in the liver and tissues responsible for the splitting up of the proteins and for reconvertng them into tissue proteins. There is some evidence to suggest that the enzyme systems in inanition cases are not normal, and that the benefit with serum may not be attained to the same extent as with hydrolysates. This theoretical explanation is supported to some extent by actual experience with serum in starvation cases.

We are inclined to believe that administration of glucose protein hydrolysate intravenously to cases of inanition is superior to the administration of serum. The marked and rapid improvement noted in most cases denotes that the amino-acids and peptides in the mixture reach all tissues simultaneously and are being utilized by them very rapidly. The glucose present in the mixture acts by reducing liver damage and increasing its functional efficiency. It saves protein break-down and indirectly helps in the synthesis of tissue protein from the amino-acids supplied. The vitamins present help in the metabolism of glucose. These facts are the basis on which we recommend glucose protein hydrolysate treatment of advanced starvation cases.

*Glucose protein hydrolysate.*—The directions for the use of this glucose protein hydrolysate have already been published in this journal\*.

*Results of treatment.*—Up to date something like 3,000 intravenous injections have been given in cases numbering about 1,000. Owing to the fact that the work has been scattered in several different hospitals and that patients have been treated at varying stages after admission into hospitals and in varying degrees of inanition, it is very difficult to give figures for death rates and recovery rates, etc., for patients treated by this treatment and by other methods of treatment. The general experience of clinicians is that in intravenous glucose protein hydrolysate we have a very useful method of treatment, but to assess accurately its value and its limitations more work with adequate controls is needed. The experience so far gained, however, would point to the following conclusions:—

(1) The intravenous injections of glucose with protein hydrolysates are well tolerated. In very few cases has any reaction been seen which could be attributed to the injection, and even in these cases other patients tolerated injections of the same batch without reaction. Moreover, the very few reactions seen have all been mild. There seems, therefore, to be no difficulty in applying this form of treatment widely. In some cases a rise of temperature soon after injection has been due not to the injection but to malaria. The only definite contra-indication to the use of this form of treatment appears to be the presence of nephritis. In such patients bad results have been seen. In patients with pneumonia, dysentery and other infections, the intravenous injections are not contra-indicated but should be accompanied by specific treatment for the infection.

The immediate reaction to the injection is usually good, the pulse and the patient's general condition improving and, in favourable cases, the patient has later been able to take food by mouth, but in severe cases this may be only after several intravenous injections. There are, however, some cases which in spite of repeated injections show only temporary improvement. The improvement is not maintained and the patient dies. Post-mortem examinations have revealed that in most of these patients there has been a serious complication such as pneumonia, malaria, severe anæmia, nephritis and, most common, dysentery with extensive bowel ulcerations. It is believed that with the use of this form of treatment a number of deaths in hospitals caused by inanition alone can be considerably reduced.

#### *Acknowledgments*

Our thanks are due to Major-General W. C. Paton, Surgeon-General, Bengal, for giving us a grant towards cost of manufacture of the product; to Dr. J. B. Grant,

(Continued at foot of next page)

# THE OCCURRENCE OF MITES (ACARINA) IN HUMAN SPUTUM AND THEIR POSSIBLE SIGNIFICANCE

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and

V. ST. E. D'ABRERA

In this note the results of some preliminary observations on the presence of mites in human sputum are recorded. At the present stage of the investigations, the presence of mites of various species has been detected in the sputum of 17 out of 28 persons examined. Twenty-four of these persons were under observation or receiving treatment for respiratory disorders in a local hospital; they were of several different nationalities and none had resided in Ceylon for more than a few months. The remaining four persons (three Europeans and one Ceylonese) had lived in Ceylon for periods of from three to over twenty years; all of them gave histories of long-standing coughs and asthma.

## Precautions against contamination of sputum samples

The presence of mites was first observed during the examination of a sample of sputum, from one of the hospital cases, for tubercle bacilli. This led to the examination of further samples of sputum from the same case, and from other cases suffering from chest complaints. The results were remarkable, and mites were found with such frequency that contamination

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Director, All-India Institute of Hygiene and Public Health, for constant encouragement and help; to Dr. B. Mukherjee, Director, Biochemical Standardization Laboratories, for testing our products and certifying its non-toxicity; to Dr. Aich of Campbell Hospital and Dr. C. R. Das Gupta of the School of Tropical Medicine and to all other doctors of emergency hospitals for trying out our product on their cases and sending us the results; lastly, to Dr. P. N. Bose of our Institute for acting as liaison officer between us and the various hospitals.

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from outside sources was seriously suspected. This suspicion was increased when it was found:

(a) that the mites which were being recovered from the sputum were not related to those species which are known to be true parasites in the lungs and air passages of monkeys and certain other mammals, but were species which are commonly present in stored products and debris in houses, shops, etc.;

(b) that mites of various kinds were present in dust and brushings obtained from the hospital and laboratory premises;

(c) that at least one of the mites present in the sputum samples was air-borne in the wards.

At an early stage in the investigations, therefore, precautions against contamination were taken whenever practicable, and results from samples of sputum to which the least doubt attached regarding the efficiency of such precautions were registered separately. In all cases in which the precautionary measures were considered to have been satisfactory, the samples of sputum were discharged direct into large test-tubes or screw-capped bottles which had been previously prepared for the purpose. These test-tubes and bottles had been thoroughly washed and cleaned and subsequently flushed for 5 minutes in running water. The tight-fitting rubber stoppers of the test-tubes and the caps of the bottles were subjected to the same treatment; they were removed only at the time of expectoration during which they were held in the hand, and after which they were immediately replaced.

Controls, using distilled water without precautionary measures, were carried out at times when specimens of sputum were being collected; and vessels containing distilled water were exposed overnight in the vicinity of mite-infected patients, and in other parts of the wards and in the laboratory. No mites were observed in any of these experiments.

The possibility of the mites being derived from the mouth or nasal passages of the patients was also investigated, and several samples of saliva and nasal washings were examined. So far, however, no mites have been recovered from these samples.

As previously stated, the results obtained from the samples of sputum taken with precautions of doubtful efficiency were registered separately. An analysis of the examinations made gave the following data:—

Efficiency of precautionary measures doubtful	..	..	63 samples
Number with mites	..	..	25 (39.7 per cent)
Efficiency of precautionary measures not in doubt	..	..	44 samples
Number with mites	..	..	21 (47.7 per cent)

Mites occurred, therefore, in both types of samples and were actually more prevalent in samples collected under precautions which rendered chances of contamination from outside



sources extremely remote. This latter fact however has no significance since precautionary measures were, in many cases, most strictly applied when there were reasons for suspecting the presence of mites. It may also be noted that the samples in the first category included 17 from 11 persons in whom no mites were found at any time; and that in all persons in whose sputum mites were originally found, the finding was subsequently confirmed in sputum samples collected in the manner described above.

In view of these facts, it is believed that while contamination of unprotected sputum samples by mites from outside sources is a definite probability and may have occurred to a limited extent in some of the samples examined, it is a remote possibility in protected samples collected as described above, and could not *per se* provide an explanation of the findings recorded. Indeed, we consider that the evidence obtained (*see* also case 3, page 166) leaves no room for doubt that in some cases at least the mites were derived from the lungs and/or bronchi of the persons under observation.

#### Method of examination

Mites or portions of mites were first seen in smears of sputum obtained by the flotation method (Proctor, 1941) used for the detection of tubercle bacilli. These specimens, however, were much distorted and too badly damaged to allow of identification. Fresh sputum was then examined under the binocular microscope, and occasional mites—sometimes embedded in plugs of mucus—were found. This, however, was a very laborious and objectionable proceeding and was discarded as unsuitable for routine purposes. The method subsequently was as follows:—

The fresh sputum was treated in the first place with an equal quantity of 1 per cent potassium hydroxide; this was shaken and allowed to stand until the mucopurulent material had disintegrated. After a few hours, when the mixture had become more or less clear, from 5 to 10 drops of Löffler's alkaline methylene blue were added and the solution again shaken. Formalin sufficient to give a 10 per cent concentration was then introduced, and the mixture left until the next morning (18 to 24 hours). The mixture was then centrifuged and the supernatant fluid drawn off; the deposit was examined under a binocular microscope.

Throughout the whole of this procedure every care was taken to ensure that no contamination with mites from the reagents or vessels used occurred.

By this process the mites were well stained and showed up clearly; they were picked up on a very fine spatula (made of platinum or silver wire) and placed in a 10 per cent solution of potassium hydroxide in an excavated slide in order to clear. The initial examination of the mites was done while they were still in the caustic potash; the mites being mounted in excavated slides, no distortion due to pressure occurred, and manipulation of the coverslip readily enabled the specimens to be studied from any desired angle. In cases where the clearing

of the mites by caustic potash was not successful, further treatment with glacial acetic acid often produced the desired effect.

When permanent preparations were required the mites were treated as follows:—

They were transferred to distilled water and subsequently to glacial acetic acid for 2 or 3 minutes, and then placed in a weak solution of carbol fuchsin—15 drops of the stain to 15 c.cm. of distilled water—and kept under observation until the desired degree of staining had been reached. The specimen was then removed to a flat slide and mounted in a medium consisting of gum arabic (30 grammes), glacial acetic acid ( $\frac{1}{2}$  c.cm.) and distilled water (60 c.cm.). This medium hardened and set in from 24 to 48 hours in Colombo.

#### Types of mites present in the sputum

It is not proposed in this note to give detailed descriptions of the various mites found in the sputum, or to attempt any pronouncement upon their specific identification. Such identification requires further research and access to literature which is not available at the moment. Nevertheless a careful study of the numerous specimens obtained has led to the conclusion that at least ten species of mites are represented in the collection.

The majority of the specimens recovered from the sputum samples belonged to the genera *Tarsonemus*, *Tyroglyphus* and *Carpoglyphus*; but a species of *Glyciphagus* was present in two samples, of *Cheyletus* in one sample, and species referable to three unidentified genera in six samples.

Two species of *Tarsonemus* were found. The larger of these occurred in one sample only, but the smaller species was the most prevalent of all mites found in the sputum of the persons examined. It was present in 41 (75.9 per cent) of the 54 samples in which mites occurred. Both sexes were observed, but the males were much less frequent, being found in four (7.4 per cent) samples only. No eggs, larvae or nymphs of this species were seen in the sputum. This mite is minute, the females ranging from 120 to 145 microns in length, and the males—which differ greatly from the females in appearance—from 90 to 115 microns. From the description of the male given by Hirst (1920) it appears to be closely related to *T. floricolus*, a species credited with a wide range of habitats including flowers, galls, decaying substances and the human urinary tract. Adults of a species of *Tarsonemus* indistinguishable from that present in the sputum were also found in dust and in the air of the wards and laboratory. Small samples of dust were collected from a variety (66) of situations in the wards and laboratory of the hospital. In the entomological laboratory, in houses and small shops ('boutiques') in Colombo, and in rest-houses in different localities. The *Tarsonemus* occurred in 15 per cent of the samples of dust examined, the infested samples including brushings from furniture and bedsteads in the wards and some of the rest-houses. From one of the samples—a small piece of fluff from the inside of the spring of a wire mattress of a bed used by one of the mite-infested patients—as many as 28 mites were obtained; 12 of these (11 females and one male) were apparently identical with the smaller of the two species of *Tarsonemus* found in the sputum. On four occasions, air was extracted from the wards and laboratory of the hospital by means of a filter pump using distilled water, and it was estimated that approximately 5 or 6 cubic feet of air were extracted in each experiment. The same species of *Tarsonemus* (in all 4 females) was recovered from the distilled water in two of the experiments.

The so-called Tarsonemid mites include many forms with widely diverse habits and modes of development, and many species which are of considerable economic importance. In Ceylon, the species *T. translucens* is an important pest of tea bushes, and elsewhere various species have been recorded attacking rice, grasses, pine-apples, sugar-cane, and other crops. *Pediculoides ventricosus*, also a Tarsonemid, commonly feeds upon insects living in grain, straw, etc., but sometimes attacks persons handling infested materials, producing a dermatitis usually known as 'grain itch' or 'straw itch'. Other members of this group of mites are parasitic in the respiratory system of honey-bees and grasshoppers, and, in the former, cause the serious condition known as 'Isle of Wight' disease.

Mites of the genera *Tyroglyphus*, *Carpoglyphus*, and *Glyciphagus* were found in 15 samples of sputum all but one of which were obtained from the same person at different times.

The species of *Tyroglyphus* found was apparently *T. longior*; single specimens of this mite were obtained in each of 10 samples of sputum, the specimens being 1 larva, 3 nymphs, 4 females, 1 male, and 1 nymphal skin. A species of *Carpoglyphus*, closely allied to or identical with *C. anonymous* Michael, occurred in 2 of 25 samples of sputum examined from the same person (case 3, see p. 166); 26 specimens, or portions of specimens, of this mite were found in the third and seventeenth samples (interval 38 days); 25 of these specimens were present in the latter sample which was obtained a day after the patient had been treated with stovarsol. These 25 specimens were as follows: 10 larvæ, 4 nymphs, 3 females (two of which contained eggs with well-developed larvæ), 2 males, and 6 adults in which the capitulum and first and second pairs of legs only were present and the sex indeterminate. Three specimens, a larva and two nymphal skins of a species of *Glyciphagus* were also found in samples of sputum from this case. Eggs—apparently of *Tyroglyphid* mites—were found in sputum on two occasions.

The genera *Tyroglyphus*, *Carpoglyphus* and *Glyciphagus* are all contained within the family *Tyroglyphidae*, and include the well-known cheese and sugar mites. Several of the species are very abundant and of much economic importance. They frequently swarm in great numbers in stored products and may cause considerable damage. Michael (1901-03) states that they 'swarm in houses generally', and are carried by 'wind, water and other agencies'. Hirst (1920) notes that persons whose work brings them into contact with materials infested with these mites are apt to suffer from forms of dermatitis variously known as 'grocers' itch', 'copra itch', 'Vanillisme', and 'water itch'. Few of these mites are parasitic, but there can be no doubt that they are often ingested by human beings and may (Hase, 1929) produce disorders of the stomach and intestine. They have also been occasionally recorded from the human urinary tract.

The record of *Cheyletus* from the sputum is remarkable as the mites of this genus are predatory and solitary in habit; they are, however, often associated with and often prey upon the *Tyroglyphid* swarms. The single specimen seen was found in the sputum of a person who was receiving treatment with stovarsol; it measured 405 microns in length and although in a macerated condition was readily recognizable.

It is not possible yet to offer any comments upon the unclassified mites found in the sputum. All that can be said at present is that eight specimens representing at least three genera were found in six samples of sputum from five different persons; single specimens of one of these species occurred in samples from three persons.

#### Observations on the findings and some case histories

In all, the sputum from 28 persons was examined, but in 12 of these circumstances

permitted of very few (one or two) samples being taken. Eleven of the latter, from whom 19 samples were procured, showed no mites in the sputum. From the remaining 17 persons, 120 samples of sputum were examined, 32 of which were obtained from six cases subsequent to treatment with arsenical preparations. Mites were observed in 46 (52.3 per cent) of the 88 samples taken prior to any of the cases receiving treatment. Usually the mites in these samples were very scanty, the largest number recorded from any single sample being four; in the majority of instances one mite only was found in a sample. In eight of these 17 persons (22 samples examined), mites were seen once only, and in six of them the small species of *Tarsonemus* was the only mite found. In the remaining nine persons (66 samples), mites were present in from two to nine of the samples taken from the same individuals; *Tarsonemus* was found in every patient, but in no case was it the only species present. Records from the three individuals from whom the largest numbers of samples were taken were as follows:—

(a) Period of observation—36 days; number of sputum samples examined 16; number of samples with mites 9; largest number of successive samples without mites 2.

(b) Period of observation—65 days; number of sputum samples examined 13; number of samples with mites 7; largest number of successive samples without mites 4.

(c) Period of observation—20 days; number of sputum samples examined 10; number of samples with mites 4; largest number of successive samples without mites 3.

From the six persons who later received treatment with arsenical preparations, 37 samples of sputum were examined prior to treatment and 32 samples subsequent to treatment. Of the former 23 samples (62.2 per cent) showed mites, whereas of the latter only 8 samples (25 per cent) were positive, and in several of these the mites appeared to be in a partially macerated condition.

Reference has already been made to the fact that all the persons who came under observation were suffering from chest complaints. In several of the hospital cases in whose sputum mites were found, the patients were discharged following improvement of their condition, or were invalided when considered necessary by the hospital authorities. In a limited number of cases, however, it was found possible to extend the observations. Examination of the blood of ten of the hospital cases and three of the private cases was undertaken; in five of the former the blood picture was normal, and no eosinophilia was observed; in five others (including one private case) an eosinophilia of from 6 per cent to 12 per cent occurred; and in the remaining three an eosinophilia of from 38 per cent to 66 per cent

was found. Brief histories of these three cases are of interest:—

**Case 1.**—O. H., British, male, aged 42 years. Commenced having asthmatic attacks in July 1943, usually in the afternoon and evening. Blood examination 16th October, 1943: W.B.C. 14,000; eosinophils 38 per cent. *Trichuris* ova present in stools. Female of *Tyroglyphus longior* found in sputum at third examination. Treated with stovarsol, grains 10 daily from 18th to 27th October, 1943. No mites observed after treatment. X-ray 3rd November, 1943: general increase of striae and slight congestion of both bases. No evidence of tuberculosis. Blood examinations 3rd November, 1943, 12th November, 1943, and 16th November, 1943: W.B.C. 18,600, 13,600 and 12,600; eosinophils 36 per cent, 18 per cent and 16 per cent. Condition improved—no attack of asthma for last thirty days.

**Case 2.**—E. B., Indian, male, aged 39 years. Chronic bronchitis and low-grade pyrexia, cough and pains in chest for 2 or 3 months prior to entering hospital. X-ray suggestive of pneumoconiosis. Blood examinations 3rd September, 1943, and 11th September, 1943: W.B.C. 21,400 and 25,600; eosinophils 66 per cent and 58 per cent. Ova of *Enterobius vermicularis* present in stools. Sputum—4 samples examined, 3 with *Tarsonemus* (small species). Commenced treatment with N.A.B. on 12th September, 1943, in all seven doses, 245 grains over a period of three weeks. Subsequent samples (5) of sputum showed no mites except that of 29th September, 1943, in which a female of the large species of *Tarsonemus* was found. Blood examinations 22nd September, 1943, 1st October, 1943, and 9th October, 1943: W.B.C. 20,600, 12,000 and 11,200; eosinophils 60 per cent, 36 per cent and 11 per cent. Condition improved subsequent to treatment.

**Case 3.**—S. J., Ceylonese, female, married, aged 22 years. Admitted into a civil hospital 16th April, 1943, with history of pain in throat, cough and evening temperature of three weeks' duration. Examination showed follicular tonsillitis, swab negative to *B. diphtheriae*; chest resonant on percussion, breath sounds harsh with expiration prolonged; adventitious sounds—an occasional crepitation over right apex and rhonchi scattered. Cough troublesome at night, night sweats, evening temperature ranging from 98.6°F. to 99.5°F. X-ray 16th April, 1943: revealed patchy infiltration of both lungs, 'the appearance being suggestive of pulmonary tuberculosis'. Sputum examined for tubercle bacilli on five occasions between 17th April, 1943, and 26th April, 1943—all specimens were negative. Blood examination 19th April, 1943: W.B.C. 21,000; eosinophils 42.0 per cent. Faeces showed no worms; urine without deposits, normal. Treatment consisted of prosectatine orally, expectorants, iodide mixture, Mandel's paint for tonsils and creosote inhalations at bedtime. The patient had been previously admitted into the same hospital for Caesarean section (21st September, 1942, to 17th October, 1942), pelvic cellulitis (22nd October, 1942, to 10th November, 1942), and appendicectomy (1st February, 1943, to 17th February, 1943). Blood examinations were made on 22nd October, 1942, and 1st February, 1943: W.B.C. 8,200 and 12,000; eosinophils 3 per cent and 8 per cent.

After discharge from hospital on 27th April, 1943, the patient moved to Colombo. The chest trouble and cough continued, and she was under medical observation and treatment for bronchial asthma. Attacks of asthma occurred at least twice a week, and night cough was often severe causing loss of sleep and lassitude on rising. Samples of sputum were first examined for mites early in September 1943; between 8th September, 1943, and 15th October, 1943, sixteen samples were examined and mites (*Tarsonemus*, *Tyroglyphus*, *Carpoglyphus* and an unidentified species) were found in nine samples. A differential blood count made on 13th September, 1943, gave an eosinophilia of 55.2 per cent. Treatment with stovarsol was commenced on 18th October, 1943, and was continued for 8 days (grains 10 on the first 2 days and grains 5 daily thereafter). All sputum expectorated after the first

dose, including that of the early morning of 19th October, 1943, was collected in a prepared tube and examined. No less than 29 mites—mostly *Carpoglyphus*—in all stages (see p. 165) were found in this sample. Eleven samples were taken subsequently (between 20th October, 1943, and 30th October, 1943) and eight mites of various kinds in a more or less macerated condition were found in six samples; the last three samples were negative. Differential counts made after commencement of treatment gave the following results: 22nd October, 1943—eosinophils 56.0 per cent; 1st November, 1943—eosinophils 18.2 per cent; 25th November, 1943—W.B.C. 8,000; eosinophils 20.0 per cent. By the end of November the patient's condition showed definite improvement, and she was 'feeling herself again'. The cough had ceased and no attack of asthma had occurred since the treatment with stovarsol.

#### *The possible significance of mites in the sputum*

Endoparasitism by mites in man has so far received relatively little attention, although mites are not infrequently present in human faeces and have occasionally been found in the urinary tract. Indeed, so far as we are aware, such endoparasitism has been specifically noted in man only in relation to infestation of the alimentary and urinary tracts, and we have failed to find any direct reference to infestation of the human respiratory system or to the presence of mites in human sputum. Endoparasitism of the respiratory system by mites is, however, known to occur in insects, birds, reptiles, and some mammals; and in certain Old World monkeys, mites of the genera *Pneumonyssus* and *Pneumotuber* are true parasites, infesting the lungs and air passages (pulmonary acariasis), and are capable of causing serious pathological conditions. As previously stated, however, the mites found in the sputum of the persons examined were not related to those parasitic in the lungs of monkeys, but were mainly of non-parasitic types which normally occur in stored products, decaying substances, and debris of various kinds. Nevertheless, it is particularly to mites of this type that the literature on endoparasitism in man relates.

Invasion of the human alimentary and urinary tracts by *Tarsonemid* and *Tyroglyphid* mites is believed to have been responsible in some instances for such disorders as gastro-enterocolitis, nocturnal enuresis, haematuria, and albuminuria. Dickson (1921) investigated two cases of infection of the urinary tract—one by *Tarsonemus* and the other by *Tyroglyphus (Aleurobius) farinae*. In the latter case the urinary symptoms had lasted many years and were supposed to be due to chronic Bright's disease; on cystoscopic examination *T. farinae* was found, especially in the trigone of the bladder. Mackenzie (1922) gave particulars of seven cases of invasion of the urinary tract by *Tarsonemus* and concluded that 'certain urinary disorders may be due to mites living parasitically in the mucous membrane of the urinary tract'. Hase (1929) in a review of the literature of the subject with special reference to *Tyroglyphidae* stated that disorders of the stomach and intestine caused by mites that infest stored products may in some cases be allergic and in others due to general toxic effect. He considered that symptoms of allergic disease caused by mites were usually associated with either the skin or the respiratory system, and that mites in houses and stores were a definite danger to health. Korkhaus (1933) in a further review of the literature relating to the parasitic and pathological

importance of the Tyroglyphidae in animal tissue concluded that though these mites are not true parasites in such tissue, they may, when ingested with food, produce both in man and animals pathological symptoms of an allergic type. In relation to respiratory diseases Ancona (1923) noted that many workers in the grain mills at Barberino suffered from asthma together with a dermatitis of the neck, chest and arms; he attributed these troubles to the mite *Pediculoides ventricosus* which was present in the grain of those mills where the workers were affected, and suggested that the symptoms were probably the result of inhalation or the action of the mites on the nasal mucous membrane. von Lengerken (1929) quoted cases of sickness and death in horses caused by feeding on mite-infested maize; the symptoms included inflammation of the respiratory and digestive organs and lameness. Examination of the infested maize showed *Tyroglyphus (Alcurobius) farinæ* to be the commonest mite present, although *Glyciphagus domesticus* and *Cheyletus eruditus* also occurred.

We have already given reasons for our belief that in many cases at least the mites observed in the sputum of the persons examined were derived from the lungs and bronchi. That they have not been previously detected is probably mainly due to the methods ordinarily used for the examination of sputum. The chances of finding a mite in a smear made from a minute quantity of sputum—particularly when the examination is for tubercle bacilli only—are exceedingly slender; for even when collections consisting of 5 c.cm. to 40 c.cm. of sputum were examined as described above, it was unusual to find more than one or two mites in any one sample.

If our view that the mites were derived from the lungs and bronchi be correct, the questions which immediately arise are those concerning the mode or modes of infection and the duration of the infestation.

Upon the first of these points we can offer no direct evidence in respect of any of the cases observed. But the observations of other writers and the demonstrations referred to in this paper of the presence of mites in the dust of wards, bedrooms, and similar places, and in the air, suggest strongly that an important, if not the chief, avenue of infection is through inhalation. The liability to infection by this method would obviously be increased in situations such as stores, mills, barns and ill-kept or dilapidated houses when, as so often happens, Tyroglyphid and other mites are present in large numbers. But the possibility of inhalation of mites from unusual or unsuspected sources must also not be overlooked. Sweet-smelling flowers sometimes harbour mites; and in Colombo we have observed a species of *Tyroglyphus* swarming on the so-called 'Temple-tree flower' (*Plumeria acuminata*) so abundantly used for religious and ornamental purposes and for garlands. That infection of the respiratory system by indirect routes following ingestion of mites with food could occur seems unlikely, but Patton and Evans (1929) have suggested that the source of *Tarsonemus* in cases of infection of the

bladder may be the rectum, and that mites may have burrowed through the tissues.

It is probable that in some cases the endoparasitic infection by mites is of a transient nature, but the histories of some of Carnegie Dickson's and Mackenzie's cases, and of case 3 above, indicate that in some instances the period of infection may be much prolonged. In our view the evidence accumulated regarding case 3 suggests strongly that the infestation had lasted for a period of not less than seven months, and that the mites had adapted themselves to the conditions existing in the lungs and bronchi. The presence of these mites (*Tyroglyphus* and *Carpolyphus*) in considerable numbers in the sputum in all stages from eggs to adults of both sexes (including egg-bearing females) cannot, we suggest, be explained on any grounds other than that of these mites breeding in their unusual habitat.

Finally, it is important to consider whether the mites were living as commensals or as parasites. The existence of a considerable leucocytosis and eosinophilia in some of the cases has already been noted; and in case 3 at least, the blood conditions suggested the presence of endoparasites which the examination of the faeces and urine failed to reveal. The high eosinophilia observed (42 to 55 per cent before treatment) could not be explained if the reaction to the mites was purely mechanical as in the case of inert foreign matter. In this connection it is of interest to note that a condition 'characterized by massive eosinophilia with focal broncho-pneumonic infiltrations affecting both lungs, and general symptoms such as fever and loss of weight' (Chaudhuri, 1943) has recently attracted much attention in India; and that several writers on the subject have stressed the necessity for its recognition and differentiation from tuberculosis. Fridmott-Möller and Barton (1940) who described it as a 'pseudo-tuberculous condition associated with eosinophilia,' studied many cases almost all of whom had the usual symptoms of tuberculosis although few showed tubercle bacilli in the sputum. They considered that the lung condition 'characterized by an evenly distributed extensive mottling of small nodular shadows over both lung fields, with increased linear markings,' was not due to tuberculosis and was probably allergic in origin. Weingarten (1943) described what was evidently the same condition as a new disease entity which he termed 'tropical eosinophilia,' and other authors have discussed it under the names 'eosinophil lung' and 'benign eosinophil leukaemia'. Weingarten's 'tropical eosinophilia' was characterized by definite bronchial and pulmonary conditions and a massive eosinophilia unassociated with the presence of internal parasites as shown by examination of the blood, faeces and urine. He considered that the disease was benign but could last for many years, and that many cases had previously been diagnosed as pulmonary tuberculosis or chronic bronchial

asthma. Arsenical preparations were ultimately found by this author to be the most effective form of treatment and to be followed by a remarkable fall in the eosinophilia; and this discovery was subsequently confirmed by other workers.

The aetiology of this variously named condition has hitherto been regarded as obscure, but in view of our findings and of the results obtained from the administration of arsenic—pre-eminently a parasitocidal drug—we suggest that the condition may be due, in part at least, to mite infestation of the respiratory system.

### Summary

1. The occurrence of mites in the sputum of 17 out of 28 persons suffering from respiratory disorders is recorded.

2. Some of the mites found in the sputum were also shown to be present in dust and in the air, and contamination of the samples from outside sources was suspected. The precautions to prevent contamination, and the methods of examining the sputum and the mites are described.

3. At least ten species of mites, some of which have not yet been identified, were found in the sputum. Those identified were not parasitic types, but were species which are commonly present in stored products and debris of various kinds. They included species of *Tyroglyphus*, *Carpoglyphus*, *Glyciphagus*, *Cheyletus* and *Tarsonemus*.

4. Prior to treatment with arsenical preparations, mites were found in small numbers in approximately 50 per cent of sputum samples taken from the mite-infested persons. After arsenical treatment the numbers of mites found in the sputum diminished, and many of those seen appeared to be in a macerated condition.

5. In three of the mite-infested persons, an eosinophilia of from 38 per cent to 66 per cent was observed. In all of these, the chest conditions improved and the eosinophilia was much reduced following treatment with arsenic.

6. In one case, 29 mites, mostly *Carpoglyphus*, in all stages, were expectorated immediately following the initial dose of stovarsol.

7. It is considered that the evidence obtained suggests strongly that the mites observed in the sputum were derived from the lungs and/or bronchi, and that in one case at least the mites had adapted themselves to the conditions present and were breeding therein. The evidence also suggests that the chief method of infection is by inhalation, and that infestation may in some cases be of prolonged duration. The view is advanced that the condition variously known as 'pseudo-tuberculosis', 'eosinophil lung', 'tropical eosinophilia', etc., may, in part at least, be explained on the basis of mite infestation of the respiratory system.

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## RECENT EXPERIENCES IN THE SYMPTOMATOLOGY AND TREATMENT OF PLAGUE

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AFTER nearly 20 years, bubonic plague broke out in this town in the middle of June 1943. It continued for nearly four months, and 210 people died from it. The municipal council erected a temporary hospital for the isolation and treatment of plague patients and I was entrusted with the charge of this hospital. One hundred and fifty-one patients received treatment in hospital, and 139 patients were treated by me in their homes.

Administration of sulphonamides by oral and parenteral methods was the chief form of treatment adopted. Preparations of sodium sulphapyridine, sulphapyridine, and sulphathiazole were

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### Acknowledgments

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used. This treatment was supplemented by neutral iodine given intravenously; 1 c.cm. being given daily with 20 c.cm. of glucose. In severe cases the following course of treatment was adopted: a large initial dose of one of the three sulphur preparations mentioned, 3 to 4 tablets, was followed by a maintenance dose every 4 hours, day and night. Ordinarily on the first day  $7\frac{1}{2}$  grammes were given, on the 2nd and 3rd days 4 grammes, 4th, 5th and 6th days 3 grammes with a total of 24 grammes. As improvement occurred, the interval was lengthened but the treatment was continued until convalescence was established. Three grains of sodium bicarbonate was given with every tablet of the sulpha preparation used in order to minimize vomiting.

In some cases, intravenous injections of M&B soluble 693 or solusceptasine were given twice daily for 6 days.

In children the dosage was reduced.

*Types of cases.*—The patients came under treatment at different stages, most of them in the stage of adenitis with hyperpyrexia, stupor, severe headache and toxic symptoms well established. Vomiting and diarrhoea were present in 25 per cent of the cases. Signs of hæmorrhage, hæmatemesis, hæmoptysis, hæmaturia or abortion were noticed in 10 cases. The primary lesion at the site of the flea-bite was noticed in 4 cases. Cases of septicæmic type without any trace of glandular involvement even after death formed about 4 per cent of the total. Even from the onset of the epidemic, cases of ambulatory type were common and in my series of 290 cases formed 7.5 per cent. One curious symptom, aphasia, was found in 4 cases. Two were seen in young boys.

The following are the case notes of a typical case of bubonic type in a young pregnant woman:—

A young woman, aged 22 years, not vaccinated for plague, 6 months' pregnant, came under treatment with high fever  $104^{\circ}\text{F}$ . to  $105^{\circ}\text{F}$ . temperature, pulse 120 to 130, respiration 36. Pneumonic consolidation of the base of the right lung with cough and rusty sputum was noticed. On the 4th day the congestion was clearing and on the 5th day pain and swelling in the right cervical gland were noticed which gradually increased in size and tenderness. On the 10th day, the patient was restless and delirious manifesting symptoms of miscarriage, which was effected at 5 a.m. the next day, accompanied by severe hæmorrhage. The maximum temperature came down to  $103^{\circ}\text{F}$ . and pulse 120, respiration 30. Swelling of the femoral glands, of the size of an orange on either side, was noticed, the lung having completely cleared on the 22nd day; temperature came down to  $101^{\circ}\text{F}$ ., pulse 100. The swelling in the femoral glands subsided but a swelling in the right calf muscle was noticed which continued for one month. This however resolved and the patient recovered. Treatment in this case was first directed towards pneumonia. Thiazamide M&B 760 tablets, 2 every 3 hours for the first day and thereafter decreasing the dose suitably every day, with an aggregate dose of 30 grammes, i.e. 60 tablets, were administered. When the cervical glands were affected, Dagenan was given. Intravenous neutral iodine 1 c.cm. with 15 c.cm. of 25 per cent glucose solution daily for one

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## A NOTE ON BACTERIUM ALCALIGENES INFECTION

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WHILE a purely clinical diagnosis of typhoid fever can sometimes be made with accuracy, it is always desirable that the diagnosis shall be confirmed by the agglutination tests and the isolation of the organisms. The present article

(Continued from previous column)

week was administered. Redoxon (vitamin C) injections also were given every third day.

The following are brief notes on a case of septicæmic type:—

A patient, aged 35 years, vaccinated against plague, was admitted into hospital on 16th September, 1943, with no bubo, but with high fever and delirium. Eyes were bloodshot, tongue dry, pulse rapid and temperature  $105^{\circ}\text{F}$ . The same line of treatment was adopted but the patient died within 24 hours of admission.

There were 9 cases of hæmorrhagic type of which the brief case notes of one are as follows:—

A patient, aged 30 years, not vaccinated, admitted into hospital with bubo in right axilla and severe prostration and high fever. He had intestinal hæmorrhage before death.

Even before the administration of sulphonamides, vomiting and diarrhoea were present in about 25 per cent of the cases. These cases were treated with intravenous injections. Six cases, apparently of septicæmic type, with no bubos, had rapidly developing convulsions and died. One case with extensive skin lesions was seen, and this patient died. There was no case of pneumonic plague but secondary pneumonia developed in 26 cases. In the 290 cases treated by me the death-rate was 42 per cent. The death-rate in the hospital was 48 per cent. This higher figure was caused by the fact that the more severe cases were admitted into the hospital. The general mortality rate in the epidemic as recorded by the Health Department was 56 per cent.

*Editorial note.*—The above paper has been considerably re-arranged and condensed by the editor.

In view of the published reports of the use of sulphonamides, particularly sulphathiazole, in the treatment of plague it must be admitted that the death-rate recorded in this epidemic in the cases so treated was surprisingly high. It would seem that this was an outbreak of plague in severe form in a population in whom plague inoculation had been little carried out, or who had been inoculated for plague too recently. Some patients were inoculated only after cases occurred in the family or neighbourhood and developed plague within a day or two of inoculation. It would also seem probable that the rather disappointing results of treatment were caused by the fact that many patients came under treatment too late. In the outbreak of plague in Nairobi in 1941 it was reported that the sulphonamides were efficacious if given early in large doses; if given later the effect was very much less.





(see figure 2) with fast pulse and hurried respiration and severe toxæmia and diarrhœa. Blood pressure 100/60 mm. of mercury. Meningeal symptoms supervened; lumbar puncture was done—14 c.cm. clear

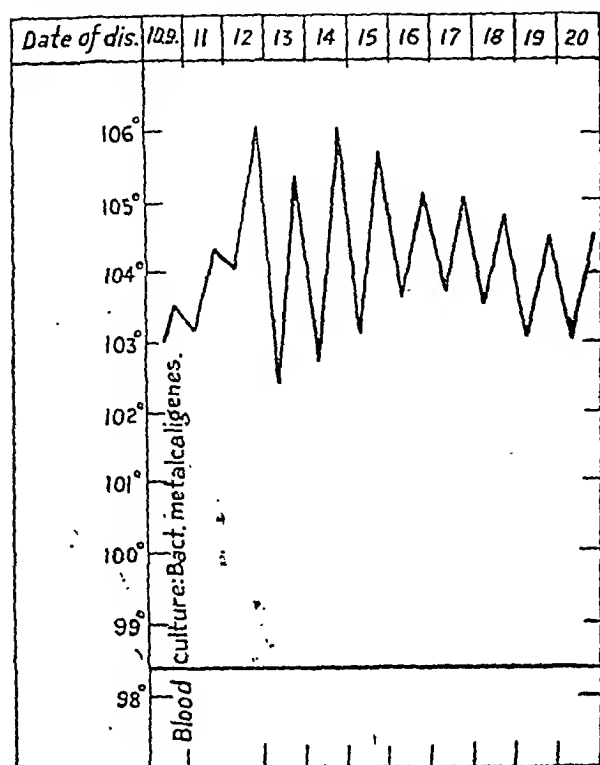


Fig. 2.

fluid were withdrawn under pressure. The patient died after 10 days, i.e. on the 24th day of illness, of terminal broncho-pneumonia.

**Laboratory findings.**—No malaria parasites were found. Blood culture showed *Bact. metalcaligenes*. Widal: TH positive 1 in 100 and To 1 in 50 only; other findings, including agglutination reaction with brucella and proteus organisms, were negative (1 in 25). Blood examinations: hæmoglobin 80 per cent (11 grammes); red cells 4,000,000 per c.mm.; ESR 38 mm. in one hour; white cells 10,500 per c.mm.; differential count—polymorphonuclear cells 79 per cent, lymphocytes 18 per cent, large mononuclears 3 per cent and eosinophil nil. From the stool *Bact. alealigenes* was isolated twice. The urine contained albumin, acetone and pus cells; the diazo reaction was strongly positive; culture showed *Bact. alealigenes*. Throat culture—streptococcus viridans and staphylococcus aureus. No abnormality was detected in the cerebro-spinal fluid; the culture showed no growth.

**Case 3.**—The third case was in an European female child, aged 4½ years, admitted on 7th January, 1943, with a history of fever for five weeks. The temperature usually rose to 101°F. to 102°F. in the afternoon, and was down to about 99.6°F. in the morning. She vomited and complained of headache during the first few days of illness. She had slight cough about the third week and conjunctivitis during the fourth week; both subsided within a short time. The general condition of the child was good. The tonsils were enlarged. The spleen and liver were not enlarged. The chest was clear. The white cell count was 20,500 per c.mm. with polymorphonuclears 77.5 per cent. No malaria parasites were found. Blood culture showed *Bact. alcaligenes*. The Widal with this organism was positive in dilution of 1 in 200 but negative with the typhoid group. The stool and urine were normal. The temperature came down after a week without any special treatment.

Three other patients (cases 4, 5, and 6) had typhoid fever diagnosed on clinical grounds with a positive blood culture in two and a positive Widal in a high dilution, in the other. They had *Bact. alcaligenes* infection as well. The main features of the six cases are given in the following table:—

TABLE

Case number ..	1	2	3	4	5	6
Patient ..	Panjabi male, age 20 years.	Bengali female, age 12 years.	European female, age 4½ years.	Bengali female, age 14 years.	Bengali female, age 14 years.	Bengali male, age 30 years.
Fever ..	Remittent in 2 bouts.	High continuous, later remittent.	Remittent	Remittent	Remittent	Remittent.
Duration ..	1st: 21 days 2nd: 31 days	24 days	42 days	29 days	25 days	30 days.
Organisms isolated from :—						
(1) Blood ..	<i>B. metalcaligenes</i> (twice) during second bout of fever.	<i>B. metalcaligenes</i> .	<i>B. alcaligenes</i>	<i>B. typhosus</i> <i>B. alcaligenes</i> <i>B. metalcaligenes</i> .	<i>B. typhosus</i> <i>B. alcaligenes</i>	<i>B. alealigenes</i> .
(2) Stool ..	<i>B. metalcaligenes</i> (twice).	<i>B. alcaligenes</i> (twice).	Negative	Negative	Negative	<i>B. alcaligenes</i> .
(3) Urine ..	Sterile	<i>B. alealigenes</i>	Not cultured	Not cultured	Sterile	Not cultured.
Widal (maximum titre).	To positive 1 in 100. Negative with <i>B. alcaligenes</i> .	TH positive 1 in 100.	TAB—negative <i>B. alcaligenes</i> positive 1 in 200.	TH positive 1 in 1,600. To positive 1 in 800. <i>B. alcaligenes</i> positive 1 in 3,200.	TH positive 1 in 400. To positive 1 in 400.	TH positive 1 in 25,600. To positive 1 in 1,600.
Result ..	Recovered	Died	Recovered	Recovered	Recovered	Recovered.

*Discussion*

Several observers have reported the isolation of *Bact. alcaligenes* from the blood of patients with symptoms suggesting enteric fever. The production of specific agglutinins in the blood to a significant titre has also been recorded in a number of cases. Ahad (1942) reviewed the literature on the pathogenicity of this organism and reported a case of cystitis due to this organism with rise of specific agglutinins in the blood. In the present series, *Bact. alcaligenes* or *metacaligenes* was isolated from the blood in six cases. The first three patients had apparently a primary infection. The agglutination reaction of the serum with the isolated organisms was negative in one and positive (1 in 200) in another; it was not done in the third case. One of the patients was seriously ill and died and the other two recovered. But for the bacteriological investigation, the diagnosis of

these three cases would have been missed and the cases classed as enteric. Cases 4, 5, and 6 had typhoid fever and these organisms which were isolated from their blood were probably concomitants. Case 4 however developed *B. metacaligenes* agglutinins in the blood, the Widal being positive in high dilution (1 in 3,200).

These observations show the importance of laboratory aid for the confirmation of the clinical diagnosis of enteric fever and for the detection of primary 'parenteric' infection that may closely resemble enteric even of a severe type. It is imperative that these cases, commonly passed as typhoid or paratyphoid on clinical grounds, should be excluded from our statistics of true enteric fever.

## REFERENCE

AHAD, N. (1942) .. *Indian Med. Gaz.*, **77**, 530.

## A Mirror of Hospital Practice

### A CASE OF SYPHILITIC MELANODERMA

By K. N. GOUR, M.D., M.R.C.P.E., F.R.F.S.G., D.C.H.,  
R.C.P.S. (Eng.), D.P.H.

Reader in Medicine, Medical College, Agra, and  
Physician, Thomason Hospital, Agra

A HINDU male, unmarried, pujari by profession, was admitted into the Thomason Hospital, Agra, on 13th September, 1941, with the following complaints :—

- (i) Pigmentation of the skin all over the body.
- (ii) Burning sensation all over the body.

The patient stated that three years back he noticed a black patch on the palm of the right hand which slowly extended above the wrist. Within two years all the extremities were practically covered with such patches. Since last year the patches have appeared and extended over the back, chest and abdomen.

A burning sensation had been first noticed in the extremities about two years back, but at the time of admission this sensation was present all over the body.

On clinical examination, no abnormality was detected in the respiratory, circulatory, gastrointestinal and nervous systems. There was no glandular enlargement and the epitrochlear glands were not palpable. The pigmented areas were a little raised and looked as if they were somewhat oedematous.

The blood Wassermann was strongly positive. A diagnosis of syphilitic melanoderma was

made and the patient was put on anti-syphilitic treatment (N.A.B. injections and iodide and mercuric mixture). The patient was discharged from the hospital on 26th November. The pigmentation had very much diminished and wherever it was still present it was slight and of a lighter shade.

The case is of clinical interest in the following ways :—

(i) The sole manifestation of syphilis was hyperpigmentation of the skin.

(ii) Such an extensive pigmentation in syphilis, covering practically the whole body, is not usual.

(iii) The appearance of the light (healthy) patches in between the large areas of dark skin was such that the impression was given that these were the diseased areas, possibly leucoderma.

(iv) The value of arsenical injections in the dermatological conditions due to syphilis is much debated, but in this case there was a rapid clearance of the pigmentation after these injections were started.

(v) There was improvement in the burning sensation produced by the anti-syphilitic treatment.

Vitamin B<sub>1</sub> was never administered.

I am thankful to Major-General H. C. Buckley, M.D., F.R.C.S.E., C.I.E., I.M.S., Superintendent of the Hospital, in permitting me to publish this case.

[Note.—In 'Modern Dermatology and Syphilology' (Becher and Obermayer), no mention is made of syphilis as a cause of melanosis.—Editor, I. M. G.]

# HIGHLY POTENT WHOLE LIVER EXTRACT

Hg %	RBC count
100	5
90	4.5
80	4
70	3.5
60	
50	
40	
30	



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# Indian Medical Gazette

APRIL

## TYPHUS FEVERS IN INDIA

Our present number contains no less than six references to typhus in India or in nearby countries, and thus gives a suitable opportunity for a discussion of this group of fevers in India.

A rather curious feature of typhus fevers in India is that far more reports of typhus fever come from the army than from the civilian population. Moreover, this is not only true in war-time when the army is relatively large, but was also true before the war when the army was relatively small. This might be understood in a country where the majority of the population live in cities but where the army might get infected in field exercises, but it is difficult to understand in a country such as India where such a large percentage of the population live in rural areas. Are we to presume that typhus is rare in the civilian population, or are we to surmise that many cases in the civilian population are not recognized? We think that the latter is probably the true explanation. This lack of recognition of civilian cases of typhus cannot be entirely explained on the basis that most of the cases occur in remote rural areas, for a considerable number of cases of typhus has occurred in the army in units stationed in large cities. It seems clear therefore that many cases of typhus in the civilian population are unrecorded, or are recorded as typhoid, and this idea receives support from the fact that many cases occurring in the army have been recognized as typhus only because the routine agglutination tests in the army include the Weil-Felix reaction, whereas in civil practice this is often not done. A careful lookout for rather abnormal cases of 'typhoid' and the more frequent doing of the Weil-Felix test will undoubtedly reveal more cases of typhus in the civilian population.

It is not proposed here to give any lengthy discussion of the typhus fevers in India. We merely wish to draw our readers' attention to some of the main facts about typhus in this country. More detailed information on the subject is given in published papers, particularly those of Megaw 1917, Boyd 1935, Heilig and Naidu 1942; a good discussion of the subject of typhus fevers in India is given by Napier in his book on 'Principles and Practice of Tropical Medicine', page 280. More information about typhus in India is now coming to light, and we hope in the near future to publish an article presenting up-to-date information on the subject mainly gathered from army sources. The following are some of the main facts about typhus fevers in India.

Epidemic typhus is found very little in India. It does occur in Kashmir, Afghanistan and other areas to the north-west, and small outbreaks

have been recorded in north-west India in the past. Epidemic typhus does not occur in the plains of India. Endemic typhus, however, is found widely distributed throughout this sub-continent. Strains of 'murine' typhus have been found affecting human beings; 'tick' typhus has also been reported from several areas; other strains of typhus showing agglutination most marked with OXK have also been reported from numerous areas. In some areas the typhus associated with OXK agglutination has resembled quite closely the mite borne, tsutsugamushi, or Japanese river fever form of typhus.

Thus probably all the different clinical and immunological types of typhus are represented in India. The typhus giving OXK agglutination apparently occurs mainly at the end of the monsoon. The murine type of typhus is apparently more evenly distributed throughout the year. The seasonal distribution of tick typhus is possibly mainly in the colder weather.

Actually in none of the outbreaks of typhus that have occurred in India has the vector been demonstrated.

On the whole, the disease in India is relatively mild, though some deaths do occur; the rash in the Indian typhuses tends to be inconstant and also may be difficult to detect in dark-skinned people. In some forms of typhus in India, the respiratory symptoms are marked, and some cases have, to begin with, been diagnosed wrongly as pneumonia. In the typhus of the Japanese river fever type, a primary ulceration at the site of infecting bite has been recorded, and glandular involvement has in some cases been marked. In some cases, the typical agglutination, particularly OXK, has been very much delayed in appearance, and may be at its height long after the fever subsided. One or more strains of rickettsiae have been isolated in animals inoculated with the blood of patients, and are now under study.

As already stated, most of the recorded cases of typhus in India have been in the army, and most of the studies of typhus in India have been done by army medical authorities. We are quite sure, however, that if civil medical practitioners will keep on the lookout for this disease in its various forms, more civil cases will be recorded, and civil medical agencies may be able to elucidate the problems of typhus in India. In the meantime, we have to thank the army for most of what we know on this subject.

J. L.

## INDIAN DEGREES FOR INDIAN GRADUATES

WE would draw the attention of our readers to the special article (page 174) on this subject, written by Lieutenant-Colonel G. R. McRobert, Professor of Medicine in the Madras Medical College.

The editor wishes to endorse very strongly almost every word of this article. This is a



matter of vital importance to the whole future of medical education and medical services in the country.

Everyone is keen to improve medical education and medical services; the matter is at present the subject of consideration by representative bodies in this country. But medical education and services will never be what they ought to be until we get really good post-graduate medical training in special subjects and really good higher qualifications widely available in this country. A start has been made in some centres. We have some excellent teachers; we have many doctors capable of benefitting from post-graduate higher studies; what we need is that the medical profession and the teaching institutions shall see the need and insist on its being met. Moreover those men who are really qualified to practise and to teach special subjects should be given the opportunity to do so.

As Colonel McRobert says, a higher qualification should be insisted on for all teaching and specialist appointments. All such appointments should be advertised, and the best applicant should be appointed.

We look forward to the day when Indian higher qualifications will command respect throughout India and abroad; when holders of such qualifications will be welcomed in large centres abroad for what they can contribute while they are studying there; and when Indian doctors will no longer go abroad to do work which they could do equally well or better in their own country, merely in order to collect a pass degree or diploma.

We hope that readers will think about this subject and give us the benefit of their views. We may refer to this matter again in our editorial columns. The medical profession in India, we feel, owes a debt to Colonel McRobert for having considered this subject so thoroughly and for having expressed his thoughts so clearly and forcibly. We hope that medical authorities of central and provincial governments and of all Indian universities will give this matter their very earnest consideration, and that, in plans for the future, this matter will be given an important place.

J. L.

## Special Article

### INDIAN DEGREES FOR INDIAN GRADUATES

By GEORGE R. McROBERT, C.I.E., M.D., F.R.C.P.  
LIEUTENANT-COLONEL, I.M.S.

*Professor of Medicine, Madras Medical College,  
Physician, General Hospital, Madras*

THE centenary of education in scientific medicine has been celebrated in several Indian universities. Practically all the principals of medical colleges in India and the great majority of the professors are graduates of Indian universities; the control of medical education in India is vested in the Indian Medical Council over which the distinguished Vice-Chancellor of the University of Calcutta presides.

Nevertheless, even today, the average Indian medical graduate seeking a higher qualification in medicine or surgery aims at a foreign diploma rather than at a higher degree from his own alma mater.

It is true that Europe and America have vast treasure houses of material and of opportunity ready for exploration. It is undeniable that it is desirable for Indian medical men and women to travel, to exchange ideas with their colleagues abroad, to see what is going on outside their homeland, and to gain experience in those departments of their science not at present fully developed in this sub-continent.

A very high proportion of the medical men who proceed overseas from India, however, do so in order to repeat study they have already

carried out here, to read up and receive coaching in elementary portions of their work, devoting their days to study with undergraduates or only recently qualified men, and, their nights in dingy lodging with fellow Indians, to mugging up coaching notes and textbooks for a fellowship of a Royal College of Surgeons or a Membership of a Royal College of Physicians, or for one, two or even more of the elementary diplomas attainable by the average young house surgeon in England at the end of a year's house surgery.

A man who goes to England merely to take a 'higher diploma' often studies only in the unit of the 'coach' under whom he places himself—generally a man of junior standing who depends on 'students grinds' for an important part of his income.

He does not see the work of the leaders of the profession, nor is his mind receptive of facts or impressions other than those likely to be regarded as orthodox and pleasing to the examiners who have to be faced.

Too often the Indian graduate embarks hastily on the first boat back to India after obtaining his parchment, and regards himself as a fully qualified surgeon, physician or specialist.

Much wasted time and money could be saved if young men and women graduates were given sound advice on the subject of post-graduate study. I am personally aware of the harm which can be done by bad counsel given in ignorance or without care.

I have known young assistants and tutors in physiology and pharmacology who have just managed to scrape together enough money to have a year or two in Europe before returning to their science departments, to be advised to go for the M.R.C.P. or F.R.C.S.; I have known a biochemist to return M.R.C.P.E., D.T.M.&H., without having visited or even seen any of the world famous departments dealing with his own subject in Cambridge, Oxford, London, Paris, Berlin or New York in which he might have spent profitable, delightful months—and all because of bad advice.

In the not too far distant future, we hope that some thousands of medical graduates will be demobilized from services, and many of those with considerable savings and a large gratuity will seek our aid with regard to 'higher studies'. Let us see to it that we teachers give the best possible advice and that every rupee is spent to the best possible advantage.

I may be asked why higher degrees and diplomas are necessary. The answer to that is that they are not necessary for everyone. A man may be a perfectly good practitioner or even a capable specialist without any higher degree or diploma. One of the most able surgeons in India holds the English conjoint diploma only: he has spent years in post-graduate specialist study in clinics abroad, but has not cared to take an examination which would guarantee to his fellow practitioners that he had submitted himself to the severe mental discipline necessary for the passing of a higher examination.

We must remember that the bachelor degrees in medicine and surgery obtained by the young graduate at the end of 5½ years of professional study, indicate only that he has absorbed the general principles of the subjects and that he has had contact with a fair sample of the various pathological conditions met with in practice.

A higher degree is intended to guarantee to the public that the practitioner has acquired skill in actual practice, has developed sound and mature judgment, and that he has acquired the habit of reading the literature concerning his profession.

The prescription of appropriate 'qualifications' for certain posts negatives tendencies to nepotism and favouritism in the filling of appointments.

The Medical Council of India has laid it down, too, that in future all teachers should have degrees. In this they were forestalled by the University of Madras which for some years has prescribed the higher degrees and diplomas and years of teaching experience required of candidates for teaching posts in colleges under its administration.

It is a curious fact that in India today it is easier to find M.R.C.P.s and F.R.C.S.s for higher posts than Doctors of Medicine and Masters of Surgery. In certain provinces the holders of Indian higher degrees are very rare indeed.

It cannot be gainsaid that the leading medical college hospitals in India are staffed by teachers of the highest quality, that their professional capacity is excellent, and that the clinical material at their disposal is unsurpassed in any part of the world, though autopsy material, which is so important for teaching, is not as plentiful as one would like.

Why then is there such a poor demand for higher degrees from Indian universities? Why this rush for the M.R.C.P. and F.R.C.S.?

One reason is that governments, railways and other employers have tended to favour Indian doctors who hold higher European diplomas but that is not the main reason. The chief cause is that the higher medical degrees of Indian universities have the reputation *amongst Indian graduates* of being so difficult to obtain that it is easier and even cheaper to go abroad for a few months and come back F.R.C.S.I. or M.R.C.P.Ed., rather than go on being failed year after year at home in India.

One has heard of examiners who insist on a minute acquaintance with the most up-to-date numbers of even quite abstruse foreign periodicals and of others who surround themselves with such an air of mystery and awe that the wretched candidates fail to do themselves justice. Some examiners have the reputation of never permitting candidates to pass at the first attempt.

I am well aware that many first-class examiners exist. I have derived great pleasure, and profit too, from association as an examiner with distinguished Indian physicians, but the fact remains that Indian higher degrees are looked upon, by many Indian graduates, as too risky to be worth while attempting. All this must go.

After nearly 20 years devoted mainly to problems connected with medical education in India and Burma, and after discussion with many teachers in this country and in Europe, I would plead for an effort to be made by all concerned to popularize our own Indian higher degrees in medicine and surgery and to have them adequately recognized by all concerned in making appointments requiring proved skill and experience.

For the higher diplomas in medicine and surgery obtainable in Europe, only a sound knowledge of basic principles is required, but that knowledge must be sound. If we could convince our own pupils in India that a firm grasp of principles combined with good judgment and with real practical experience under an able master would be rewarded by a higher degree, we should do a great deal for the country.

The fanatical—no digitalis except in fibrillation, erime ever to plug the uterus, partial gastrectomy for all peptic ulcer—type of examiner can play havoc with the pass list unless he is out-numbered by more balanced colleagues.

A meeting of representatives from the medical staffs of all the Indian universities concerned might well be arranged in order to devise means

for encouraging promising graduates to take higher degrees.

The pass standard should be that which could be attained by an average diligent—passed all undergraduate examinations at the first attempt—M.B. graduate with 3 years' experience after qualification—most of it spent in a teaching hospital. The standard should not be that of a professor or assistant professor and the candidate should be able to get his book knowledge from the latest edition of large standard textbooks supplemented by judicious reading of one standard weekly journal such as the *Lancet*. Mental indigestion results from literary voracity and all delving by degree seekers in out of the way periodicals and monographs should be discouraged.

Time for rumination and cogitation is required.

Handling of many cases and seeing patients right through their illness from the first day to complete restoration to health or to the post-mortem room, are necessary for the acquisition of that experience and judgment which is essential in the holder of a higher degree..

Let us therefore aim

(1) At laying down a standard of experience necessary. Let this be, say, 3 years in a teaching hospital after graduation or 5 years in practice.

(2) At ensuring that the candidate knows how to look up the literature of a subject and to present facts and findings in an orderly fashion and that he has made good use of his time in hospital, by insisting on the presentation of case records with full annotations and commentaries (and in surgery and gynaecology with operation records).

Only those candidates who satisfy the board of examiners in the above respects should be permitted to take the higher examinations concerned.

All papers should be valued by all the examiners independently.

In the clinical examinations, all the examiners should work together. All vivas and practicals should be conducted by all the examiners together. Cranks may even go in pairs, and it is wise, in my experience, in such higher examinations that every step in the examination be submitted to the judgment of all examiners, sitting together and discussing their differences of opinion. It is absolutely essential to foster the belief in the minds of young Indian graduates that the day of obscure questions and of prejudiced and cranky marking has gone for ever.

So far as the specialities are concerned, we have in Madras instituted one-year diploma courses in ophthalmology, obstetrics, tuberculosis and radiology, and the time has come for an extension of these throughout India and to cover all the usual specialities such as venereology, dermatology and orthopaedics. There is quite enough material in India to justify the institution of all the diplomas now given in London with the exception of a diploma in

psychiatry—a subject almost entirely neglected in this country.

For what purpose should medical men and women go abroad and why should they go?

For the aspirant to a professorship or to any senior teaching post, a period of study overseas should be regarded as essential. A worker in any branch of science in India needs 'contacts' with leading men in his own field. It is often impossible to discuss details of a special advanced piece of research with another worker in the same line in India.

If an Indian is working along certain lines, it will be much easier to submit work for criticism to a fellow worker in Zurich, Madrid, or Birmingham if he has been there in person and made 'contacts' which should be renewed and strengthened as time and funds permit.

We have in India a fine body of general physicians and general surgeons but very few specialists in subdivisions of medicine and surgery.

The number of thoracic surgeons able to perform lobectomies or even thoracoplasties with the accustomed ease which comes from frequent repetition, is small; the neuro-surgeon is almost non-existent. The number of refractionists and perimetrist in the ophthalmic world in India is astoundingly small, considering the material available; expert therapeutics of retinal detachment is extremely rare.

How many experienced endoscopists capable of reporting intelligently and with reliability on a stomach or bronchus are available in India today?

The demand for such specialists is insistent and must be supplied. It can be supplied only by Indian doctors (already thoroughly grounded in their subjects, already possessing higher degrees and the appropriate diplomas in their own country), who are prepared to put in hard work at one of the specialist clinics abroad, working perhaps for many months, for example, with a man who spends his whole working life doing bronchoscopies or radiographing the lumbar spine or canalizing the prostate.

No intensive study of books is required. In the evening and week-ends the visiting doctor should mix with the inhabitants of the country visited, make a study of their lives, their habits, their culture, music, art and literature.

He or she will return to India not only more fitted than in the past to play the part of a specialist but also with a wider knowledge of what goes on in the great world outside India.

The general physician in a big city today has a poor time unless he is a senior consultant. The public wants the specialist and means to have him. Even the poorest of our out-patients knows on what day to come if his kidneys are out of order and to avoid certain days if he has a joint or bone disease.

Two subjects cannot at present be fully appreciated by the Indian graduate without a visit abroad.

One is the wonderfully beneficial effect which a devoted, educated and capable nurse can exercise on a patient. Nursing education in India, even in pioneer Madras, is still in a very undeveloped stage, and the nursing care of patients leaves much to be desired. It is also impossible for one who has not visited Europe to imagine the high state of public health administration attained there, and post-graduate study in hygiene in Europe and America for Indian doctors is a crying need.

With regard to anatomy, physiology, pharmacology and biochemistry in India these have only recently been established as subjects in their own right.

As in Europe till the early part of this century, these subjects have been taught in medical colleges till 1928 or so by men 'passing up' to clinical teaching appointments. This arrangement, inevitable at the time, has very properly disappeared and only pure specialists in these sciences are now employed in teaching them.

The standard of heads of departments is however not universally satisfactory because Indian college authorities still prefer to promote assistants by seniority to professorships instead of advertising senior posts. Keen young pharmacologists and physiologists find it difficult to obtain advancement or to get adequate research facilities, as the existing professors and their assistants are overwhelmed with routine teaching duties to an extent quite inconceivable in Europe. Young men keen on these laboratory sciences should work for the degree of M.Sc. in their own universities and then, if possible, go abroad to a laboratory of repute where they may pursue research work under one of the many inspiring

and helpful professors who abound in Europe and America.

I should like to make some remarks about the prevailing habit of going abroad for a pass diploma in England, Scotland or Eire.

It has been an unfortunate fact that those medical men who, through ignorance, financial stringency or other cause, chose to enter the medical profession in India through the portals of a medical school instead of a medical college of a university have found themselves in a lower caste, the only hope of escape from which was a sojourn in Europe with a diploma registrable in the United Kingdom in view.

The University of Madras has for some years made it its business to help the deserving L.M.P. to rise, and I trust that before long all university bodies in India will take an active share in promoting the interests and educational uplift of this deserving class, though, at the same time, maintaining their pass standard with rigor.

Our experience has been that after stern weeding out of the unfit, those who remain to qualify for M.B.S. attain a high standard, and a number are eager to rise still further and in fact have done so.

Action on these lines will prevent waste of good money on foreign travel 'for lower studies'.

Let us get rid of the prevailing tendency to insist on overseas diplomas rather than on overseas experience, on contacts with coaches instead of creators, and with tutors in place of inspiring leaders.

Let those who sail from India do so in order to reap a rich harvest of the world's bounty of advanced knowledge rather than to scratch over the ground which they have already ploughed.

## Current Topics

### The Rickettsiae

(From the *British Medical Journal*, ii, 30th October, 1943, p. 550)

WAR and famine are usually accompanied by pestilence, and it will be surprising if the latter fails to play a part in the present world tragedy. Apart from influenza, louse-borne typhus fever probably presents the gravest menace; indeed *Rickettsia prowazeki*, its causative organism, has already given indications of its readiness to take a hand in the game. It is of some importance that we should not allow ourselves to be lulled into a false sense of security by our remarkably good health record to date or by the long freedom from epidemic typhus which this country has enjoyed; we may yet have urgent need of all the knowledge about the rickettsiae which research workers have laboriously acquired. The rickettsiae, as is well known, cause many diseases of both man and animals, apart from louse-borne typhus, and many species are simply harmless intestinal parasites of arthropods—e.g., lice, bugs, mites, ticks and fleas. The trench fever of the last world war was almost certainly a rickettsial disease; so are Q fever of Australia and Rocky Mountain spotted fever; and it is highly probable that rickettsial agents of many endemic fevers in all

quarters of the globe remain to be discovered. By far the most important, however, are the typhus group of fevers, and of these louse-borne typhus holds pride of place because it is the only rickettsial disease, except possibly trench fever, which is primarily a disease of man and hence liable to assume epidemic or even pandemic proportions. Other members of the group, transmitted by mites, ticks and fleas have animal reservoirs and tend to remain endemic so far as man is concerned, but there is evidence that flea-borne murine typhus, which has occurred within recent years in Great Britain, may mutate to the classical epidemic form provided that opportunities exist for its transmission through lice. The revelations of Kenneth Mellanby concerning the frequency of louse infestations are not without significance in this connection. It is extremely unlikely that a major epidemic will originate in this country, but conditions in parts of Europe and Asia are becoming ideal for an explosive outbreak, and M. D. Mackenzie holds the view that widespread movements of population, by introducing the disease into a typhus-free region, may be a factor equal in importance to famine and overcrowding.

There is now little doubt that the rickettsiae are living and reproductive micro-organisms. Akin to the bacteria in some respects and to the viruses in others, they constitute a sort of biological connecting group.

They are not filterable in the bacteriological sense, and are visible by ordinary microscopy, especially when stained; moreover, the recent application of electron microscopy to the morphological study of several species has revealed an organized structure within a limiting membrane. Like the viruses, however, they have so far eluded all attempts to cultivate them on lifeless media, and some species appear to be obligate intracellular parasites. Fortunately *R. prowazeki* can be grown in the yolk sac of the chick embryo and in the lungs of infected mice, and both these methods of obtaining large quantities have been applied to the production of vaccines. It is too early yet to say whether the immunity they engender affords satisfactory protection against natural infection. So far only Weigl's vaccine, prepared from the intestinal contents of infected lice, has yielded satisfactory evidence of efficacy in the field, and this method presents too many difficulties for large-scale vaccine production. The problem of immunization is one of great urgency, for as yet we possess no chemotherapeutic agent capable of influencing the course of the disease; the sulphonamides are quite useless and may actually be harmful.

As regards diagnosis we are on firmer ground. The curious antigenic relationship which exists between rickettsial species of the typhus group and certain strains of *Proteus* has provided a means of easy and rapid laboratory diagnosis. A sporadic case of typhus fever may be impossible to diagnose on clinical grounds, but the Weil-Felix reaction on a sample of the patient's serum, taken towards the end of the first week of illness, will almost certainly give a definite answer. In view of the exceptional importance of the disease at the present time it is far better that the doctor should submit a score of negative sera for laboratory tests than that he should omit to send a single positive one.

### Flavicin : A New Antibacterial Substance

(From the *Medical Press and Circular*, Vol. CCX, 8th September, 1943, p. 147)

SINCE the discovery of penicillin by Fleming, a number of investigations have been carried out on antibacterial substances produced by micro-organisms. As a result of these investigations it has been shown that besides *Penicillium notatum* other fungi and bacteria are able to produce powerful bacteriostatic and bactericidal agents. Some of these, such as gramicidin and tyrocidin, are quite toxic, whereas penicillin has almost no toxic action. Bush and Goff have now shown that *Aspergillus flavus* produces a powerful bactericidal agent similar in many respects to penicillin, which they have called flavicin. Details are given in their paper of the mode of preparation, and results of *in vivo* and *in vitro* tests. Severe toxic reactions were encountered at first, but on further purification these were eliminated. The substance is apparently an organic acid which is water-soluble and ether-soluble, and is unstable in an acid environment. It has a bactericidal action on gram-positive cocci, comparable with penicillin, but appears to be more active than penicillin against *C. diphtheriae*, *B. anthracis*, *staph. albus* and *Brucella abortus*.

### Auto-hæmolytic Anæmia with Auto-agglutination : Improvement after Splenectomy

By E. H. REISNER, M.D.  
and

M. KALKSTEIN, M.D.

(Abstracted from the *American Journal of Medical Sciences*, Vol. CCIII, March 1942, p. 313)

1. THE problem of acute hæmolytic anæmia due to auto-hæmolysins is discussed with particular emphasis on the phenomenon of auto-agglutination.

2. A review of the literature reveals 54 cases of auto-agglutination. The immunologic aspects of auto-hæmolysis and auto-agglutination are discussed and the more satisfactory concept of the auto-antibody reaction is advocated.

3. A case of acute hæmolytic anæmia with a strong auto-agglutinin is described. This auto-agglutinin was unique in that it persisted despite warming to 37°C. and could not be separated from the red blood cells.

4. In the presence of the spleen the auto-antibodies caused the destruction of blood cells introduced from without, but following splenectomy, transfusions were tolerated with rise in the blood count, despite the persistence of the auto-antibodies. It would appear from this that splenectomy is the rational therapy in such cases.

### A Note on the Rickettsioses in India

By N. H. TOPPING

R. HEILIG

and

V. R. NAIDU

(From the *Public Health Reports*, Vol. LVIII, 6th August, 1943, p. 1208)

MCGAW(1) in 1921 described a case of a typhus-like illness in India in which the tick was implicated as the vector. Since that time there have been many cases of typhus-like illness described throughout India. The vector of most of these cases could not be accurately determined and, since the cases were largely sporadic, epidemiological investigations have not been particularly enlightening in this regard. Weil-Felix studies on some of these cases, using the three standard proteus antigens OX19, OX2, and ONK, have revealed no great uniformity in results.

The rickettsioses in India, therefore, are not clearly differentiated. Apparently there is endemic (murine) typhus for Webster(2) isolated strains from wild rats that produced proteus OX19 agglutinins. Thompson(3) reported a small outbreak, probably of epidemic (house-borne) typhus, which consisted in seven cases with four deaths. Webster(2) also isolated in animals a strain of rickettsial virus from a patient who gave a high OXK agglutination. This leads one to suspect that cases of the mite-borne type, such as Malayan typhus (scrub typhus) or tsutsugamushi fever, may exist in India. Finally, there apparently are cases that cannot be classified readily by either the Weil-Felix test or by clinical or epidemiological considerations.

Two of us (R. H. and V. R. N.) have recently published studies on typhus fever in Mysore(4 and 5); the cases reported fall into the indeterminate group rather than into one of the more clearly defined groups. The clinical aspects of the disease suggest certain similarities to Rocky Mountain spotted fever in the United States. The location and other characteristics of the rash are quite similar to the Rocky Mountain spotted fever eruption; the duration of the fever is also similar. The Weil-Felix reactions in the cases were not consistent and in no reported instance were the results with OX19 comparable to the high titres seen consistently in cases of endemic typhus fever in the United States or of epidemic typhus fever elsewhere.

Bengtson has reported a technique for the preparation of rickettsial antigens to be used in complement-fixation tests(6) and has demonstrated the specificity of such tests(7 and 8). For some time the complement-fixation test has been employed at the National Institute of Health as a means of differentiating Rocky Mountain spotted fever from typhus. The test has been of decided advantage over the agglutination reaction in differentiating these ailments since both of these diseases produce a positive Weil-Felix. Neutralization tests may be employed but are more difficult to perform and require large numbers of





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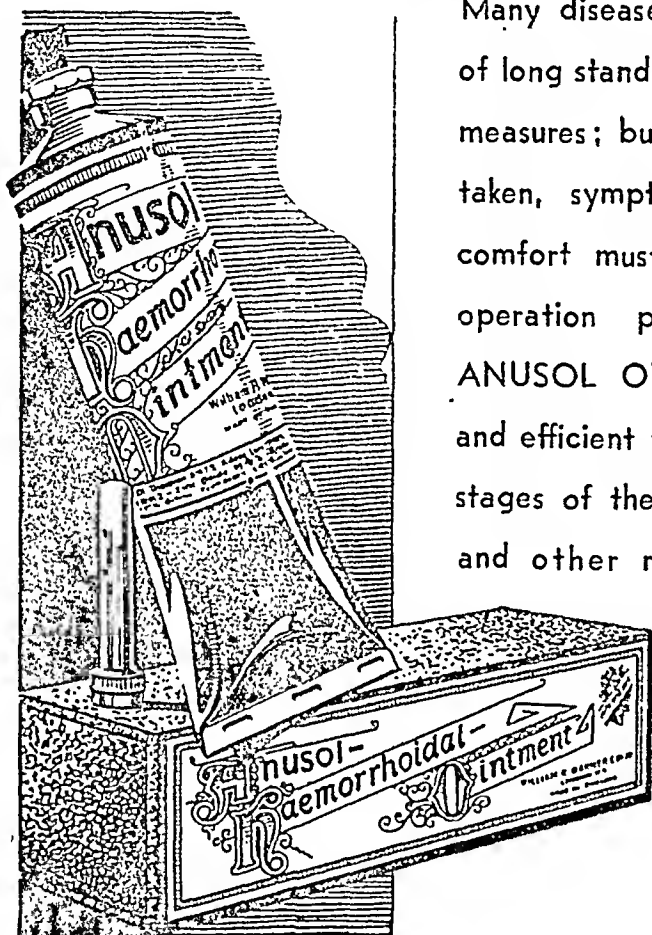
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animals, while cross protection tests entail the isolation of the causative agent which frequently is impossible.

To study further the cases of typhus occurring in India, serums from three of the most recent cases seen by R. H. and V. R. N. were shipped to the National Institute of Health for test by the complement-fixation method. The technique employed was that described by Bengtson(6). The following results were obtained :—

- (7) BENGTSON, I. A., and TOPPING, N. H. (1941). The specificity of the complement-fixation test in endemic typhus fever using rickettsial antigen. *Pub. Health Rep.*, **56**, 1723.
- (8) BENGTSON, I. A., and TOPPING, N. H. (1942). Complement-fixation in rickettsial diseases. *Am. J. Pub. Health*, **32**, 48.

#### SERUM DILUTIONS

	1:4	1:8	1:16	1:32	1:64	1:128	1:256	1:512
Case 1								
Rocky Mountain spotted fever antigen ..	4+	4+	4+	4+	2+	1+	Trace	0
Epidemic typhus antigen ..	1+	Trace	0	0	0	0	0	0
Endemic typhus antigen ..	2+	1±	0	0	0	0	0	0
Case 2								
Rocky Mountain spotted fever antigen ..	4+	4+	4+	4+	4+	4+	4+	2+
Epidemic typhus antigen ..	1+	Trace	0	0	0	0	0	0
Endemic typhus antigen ..	4+	4±	4±	3+	2+	1+	1±	0
Case 3								
Rocky Mountain spotted fever antigen ..	4+	4+	4+	4+	4+	4+	4+	1±
Epidemic typhus antigen ..	4+	4±	1+	0	0	0	0	0
Endemic typhus antigen ..	4+	4±	4±	1+	1±	0	0	0

These results indicate that the causative agent of these three cases is more closely related immunologically to the rickettsia of Rocky Mountain spotted fever than to the rickettsia of either endemic or epidemic typhus. We have no explanation for the cross-fixation at lower titres with endemic typhus antigens. We have, however, occasionally seen serums from cases of Rocky Mountain spotted fever and endemic typhus that gave cross-fixation with the other antigen, but this is not common.

From our results it would seem that there are cases of rickettsial disease in India that produce in the patient's serum high titre complement-fixation antibodies against the rickettsial antigen of Rocky Mountain spotted fever. The exact determination of the identity of this disease will depend upon the isolation and identification of the aetiological agent in laboratory animals.

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- (3) THOMPSON, T. O. Fevers of typhus group in Northern India. *J. Roy. Army Med. Corps*, **72**, 267.
- (4) HEILIG, R., and NAMU, V. R. (1941). Endemic typhus in Mysore. *Indian Med. Gaz.*, **76**, 705.
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- (6) BENGTSON, I. A. Complement-fixation in endemic typhus fever. *Pub. Health Rep.*, **56**, 649.

#### The Treatment of Uncomplicated Duodenal Ulcer

By L. A. SMITH, M.D.

and

A. B. RIVERS, M.D.

(From the *Journal of the American Medical Association*, Vol. CXXII, 22nd May, 1943, p. 209)

THE term 'uncomplicated duodenal ulcer' implies the absence of perforation, deep penetration, hæmorrhage or gastric retention. The treatment of uncomplicated duodenal ulcer is a problem which is encountered so frequently that it constitutes a challenge to the ingenuity of the medical profession. This problem becomes even more important during wartime; when the incidence of duodenal ulcer increases. Great confusion regarding treatment has arisen because of the number and variety of therapeutic methods which are perennially finding their way into medical literature. Many of these so-called improved methods live a short period and die the natural death of fads, but some members of the medical profession go on applying them even after their sponsors have discontinued their use. Certain fundamental principles pertaining to peptic ulcer are not used sufficiently in the evaluation and treatment of this disease. Too often the local lesion is remembered and the patient who harbours the disease is forgotten. In this paper we are attempting to point out how many of the known facts concerning this disease can be applied to its treatment with intelligence and efficiency.

#### DIAGNOSTIC FEATURES

Whenever a patient complains of abdominal pain or distress which is suspected of being due to duodenal ulcer, the physician should not feel solely dependent on the laboratory or roentgenologist for a diagnosis. In fact, to do so is to overlook some important diagnostic

points. Few types of pain or distress indicate the diagnosis as clearly as that which occurs with duodenal ulcer. The outstanding feature of such distress is that it is chemical in origin and is dependent on the presence of free hydrochloric acid for its initiation and behaviour. Whenever upper abdominal distress occurs at a time when free acid is expected to be at its height, namely several hours after a meal and especially at 1 or 2 a.m., and whenever this distress is relieved by measures which will dilute, neutralize or evacuate the acid chyme, a diagnosis of ulcer should be made and considered correct until proved otherwise. This diagnosis may be considered correct even though repeated roentgenoscopic examinations do not reveal the ulcer. The frequency with which early duodenal ulcer is demonstrated on roentgenologic examination varies directly with the skill of the roentgenologist, and because of the difficulties inherent in such a demonstration it is still necessary to rely on a clinical rather than roentgenologic diagnosis to determine definitely the presence of an active duodenal lesion. It must not be forgotten, however, that gastritis, especially in its erosive forms, may produce ulcer-like distress, but the presence of gastritis may be determined or excluded by gastroscopy. Aside from its chemical nature the location, radiation and intermittence of the distress are of importance in making the diagnosis.

If duodenal deformity is demonstrated on roentgenoscopic examination, the clinician should ask himself a number of searching questions. Is the deformity caused by an intrinsic gastrointestinal lesion and, if so, is it ulcer? Is the ulcer active? Is the ulcer causing the symptoms of which the patient complains? Is the ulcer associated with some other abdominal pathologic process? Is the ulcer complicated?

#### CHOICE OF TREATMENT

The capacity for healing possessed by ulcers is truly remarkable. Even when many factors promote chronicity, the natural tendency of the ulcer is to heal. It is obvious that the ideal time to heal an ulcer is early in its course. Unfortunately, many ulcers are allowed to continue because of the slight concern of the patient, the failure of his physician to recognize the symptoms early or because of ineffectual, incomplete treatment.

As a rule the following groups of patients who have duodenal ulcer should receive medical treatment first: (1) almost all those who have uncomplicated duodenal ulcers, especially those of short duration; (2) all younger patients, 30 years or less, if at all feasible; (3) usually those older patients who have more chronic uncomplicated duodenal ulcers, especially if the symptoms are mild or infrequent, not progressive and do not interfere seriously with the efficiency of the patient; (4) aged patients with duodenal ulcers, especially those who have other organic disease, such as active pulmonary tuberculosis, angina pectoris, diabetes mellitus, advanced nephritis, decompensated heart disease or obesity; (5) definitely psychoneurotic patients with duodenal ulcers; (6) hyperirritable patients with rapidly emptying stomachs; (7) patients who refuse operation even though it may be indicated; and (8) women patients whose ulcers are not complicated by extragastric disease, such as gall stones. All such patients usually do well on medical treatment.

Circumstances which indicate surgical procedures in spite of the uncomplicated nature of the duodenal ulcer are as follows: (1) ulcer of long standing with extensive chronic scarring which may make healing difficult and recurrence likely; (2) the possible association of disease in the appendix or gall bladder, or both, which is not errable by measures other than surgical; surgical exploration may reveal some extragastric factor as being more important in the production of symptoms; (3) economic conditions which make dieting impossible and make the earlier restoration to health and work following operation desirable; and (4) intractability to treatment.

After it has been decided that the symptoms are the result of a duodenal ulcer, whether or not the ulcer

is demonstrated roentgenologically, there are several essentials to success of medical treatment.

#### ESSENTIALS TO SUCCESSFUL MEDICAL TREATMENT

*Careful evaluation of all the factors which seem to promote chronicity.*—All factors which seem to promote chronicity must be evaluated carefully. This can be done in each case only by a carefully taken descriptive history which includes not only a chronologic account of the development of symptoms but also an inquiry into the possible ætiologic factors and the factors acting to keep the ulcer active.

The neurogenic factor in ulcer has been considered in other publications. Suffice it to say that this is probably the most important single factor in any case of ulcer. Its recognition is necessary first in the evaluation of symptoms. It becomes even more necessary in managing the actual healing of the ulcer, but in our opinion it offers its prime service in the prevention of recurrence of ulcer.

Chemical factors cause the greatest difficulty in the healing stage because of the lack of really adequate methods of reducing the concentration of acid to a low enough point to permit quick healing and of maintaining it at that level throughout the twenty-four hours. When a method of eliminating secretion of free acid is found, all ulcers will respond to treatment, provided mechanical obstruction is not already too great.

Infections with special affinity for gastroduodenal localization may lead to acute flare-ups of chronic ulcers, to formation of acute ulcers or even to gastritis in association with ulcers. Such infections may be acute forms, such as influenza, septic sore throat or coryza, or they may be in the form of chronic tonsillitis, peri-apical dental infection or chronic prostatitis.

Vascular changes, typified by arteriosclerosis, may reduce the nutritional supply to an ulcer enough to interfere with healing. Such arteriosclerosis constitutes a decided additional risk if the possibility of bleeding arises.

Nutritional ulcers are probably uncommon, but poverty, voluntarily restricted diets, fad diets, too strenuous ulcer diets, strictly limited allergy diets and finally anorexia nervosa at one time or another may be primary causes or may promote chronicity.

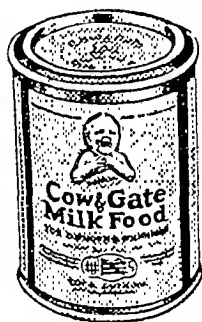
Traumatic factors are uncommon in duodenal ulcer. The best examples of such factors pertaining to peptic ulcer in general seem to be the ulcerations found in some cases of diaphragmatic hernia or in cases of bezoar. In these cases local injury certainly bears relationship to the origin of the lesion. However, flare-ups of deep chronic duodenal ulcers in farmers often occur during periods when they are riding on a tractor, and such lesions have been known to develop following blows to the upper part of the abdomen.

*Co-operation of the patient.*—The treatment of duodenal ulcer is dependent on the co-operation of the patient for its success. Because of those very qualities which may have led to his ulcer in the first place, the ulcer patient may find it difficult to co-operate. Restlessness, ambition, drive, irritability, inattention and above all, lack of desire, inability or unwillingness to learn from past experience are qualities which hinder the physician's efforts. Ulcer patients are, as a rule, intolerant of ill health and resent the fact that their activities are restricted, almost as much as they resent having pain. They seek an easy road to surcease from their problem. However, most patients who have duodenal ulcer are shortsighted and, although usually amenable to all therapeutic suggestions if their ulcers are hurting, it is difficult to make them carry on serious programmes of therapeutics when they are comfortable.

Two points should be made clear to every patient whose ulcer is going to be treated by a medical regimen. The first is that the responsibility for the healing of the ulcer belongs to him and that he should not expect to pass the responsibility to the physician, to the surgeon or to chance. The average ulcer patient welcomes any suggestion from his physician that he have an operation



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for his ulcer. Most of such patients will admit that in large part the one factor which keeps them from following directions carefully after they are comfortable is the feeling that if pain and distress ever become sufficiently intolerable they can always have the ulcer cut out and be rid of it, easily and permanently.

The second point is that the ulcer patient should realize that treatment must be directed to more than the local lesion and that even after healing of the lesion care must be used for the rest of his life to prevent recurrence. The patient, therefore, must be convinced that the healing of the ulcer and remaining free from symptoms are two entirely different achievements. Knowing this, the patient must be instructed in the rationale of the treatment so that in his daily life he will be able to anticipate the needs which arise for added care in the prevention of recurrence.

When a patient with an ulcer is seen soon after the onset of his symptoms or when he has had unrecognized and untreated ulcer symptoms for a long time, hospitalization for observation and planning of a programme is advisable in most instances. Many physicians feel that as long as symptoms can be relieved on an ambulatory programme the expense of hospitalization is not justified. However, such care in these and other types of patients with ulcer has manifold purposes: patients who are stimulated and tense may not become relaxed or co-operative otherwise; such rest and relaxation may be necessary to start healing and to convince the patient of the relation of his nervous system to his symptoms; the physician has a chance to become better acquainted with the various factors present in the personality of the individual and to investigate any possibility of obstruction; the time spent in the hospital may be used to overcome the usual reluctance of the patient to give up the use of tobacco; a definite therapeutic programme and goal may be worked out for each patient. When such hospitalization is not practical and is not demanded by the severity of symptoms, ambulatory instruction is the next best choice. One advantage which the ulcer patient enjoys in the hospital is that he usually mingles enough with other patients who have ulcers to benefit from discussion of the mutual problem. Often this tends to overcome barriers to the physician's efforts. Lectures on the subject of ulcer are of benefit in giving groups of patients better understanding of the rationale of treatment.

#### MEDICAL TREATMENT

It is clear that, while maintenance of anacidity by nearly continuous neutralization will lead to healing of a duodenal ulcer if maintained long enough, recurrences will not be prevented unless the underlying factors are eliminated. Our programme must contain more than the inevitable diet list and alkalis if success is to be maintained.

The treatment of uncomplicated duodenal ulcer then falls naturally into three parts: (1) the control of ulcer symptoms, which is usually rapid and rarely requires more than a few days; (2) the healing of the ulcer, which probably requires from twelve to twenty-four months, depending on many factors; and (3) prevention of recurrences, which requires intelligent application of individual prophylactic measures during the rest of the patient's life.

*Getting the ulcer patient comfortable.*—The measures employed in accomplishing our goal naturally vary with the character of the ulcer with which we are dealing.

Many patients who have duodenal ulcers do not have clinical symptoms. The ulcers may have been found in a search for the cause of other symptoms. However, a remote history of ulcer-like distress which indicates the past existence of activity may be obtained from these patients. Perhaps such a patient requires only a programme to prevent recurrence of activity of the ulcer.

The patient with an average amount of pain referable to the ulcer or even mild distress is treated best by

hospitalization for reasons already mentioned. No other method of teaching the patient to understand his own condition seems to work quite so well. Treatment is dependent for its success not on a routine and unvarying approach to what is always a variable problem but on the correct evaluation of the individual factors involved and institution of measures individually tailored for their correction. We have no fixed dietary programme but use a type of diet commensurate with the severity of the symptoms. The variety of foods is rapidly increased so that at the time of dismissal from the hospital the patient's programme will permit him to carry on fairly normal activity. We may start with frequent feedings of milk and cream, alternating every half to one hour with an alkaline powder or antacid, or we may even begin with a bland diet given in three meals, with milk halfway between meals. Sedatives, antacids and antispasmodics are essential adjuncts in the treatment.

When symptoms of ulcer are subacute and medical treatment is to be employed, a rigid programme in the hospital always is instituted at the Mayo Clinic. An effort is made to keep the free acid of the gastric contents at as low a level as possible throughout the twenty-four hours. Three or 4 ounces (90 to 120 c.c.) of a mixture of half milk and half cream is provided every hour from 7 a.m. to 9 p.m. On the half hours between the feedings of milk and cream we usually give either alkaline powders or aluminum hydroxide. When distress is severe during the night and this cannot be attributed to a partial duodenal obstruction with resultant hypersecretion, sedation at bedtime permits several night feedings without too much disturbance of sleep. Gastric aspiration at bedtime, followed by instillation of olive oil, also may be of service in preventing night distress. Some physicians have preferred the use of a continuous drip of milk or aluminum hydroxide through a nasogastric tube, and indeed in certain selected cases it is of great value. In most cases, however, we have found its use unnecessary. If aspiration of gastric contents shows free acid of less than 20 units a half hour after a feeding of 90 to 120 c.c. of milk and cream, the control of acid after adequate sized doses of alkaline powder or aluminum hydroxide can be assured in most instances.

*Healing of the ulcer.*—Even though a duodenal ulcer has been demonstrated roentgenographically, its activity may be questioned. When there is doubt, it is wise to determine the effect of medical treatment on the abdominal symptoms. If symptoms are relieved thereby an attempt to heal the ulcer will probably be advisable.

After the average duodenal ulcer has been brought under symptomatic control, the diet may be increased rapidly to a liberal bland diet with milk between meals and at bedtime, and antacid an hour after meals. The patient is warned of the fact that he must continue to treat himself for ulcer even though he does not have any distress. Mild sedation helps him readjust to his work, and the use of sedatives during periods of nervous tension or overloads of responsibility should be recommended.

Because of the tendency of ulcers to flare up during colds, family tragedies and the like, the ulcer patients should be forewarned to be unusually careful and, contrary to the usual tendency, to take feedings frequently, to eat lighter food and to use antacids more vigorously as a prophylactic measure during these times. The inability of many ulcer patients to learn from past experience is illustrated by the fact that most seasonal types of ulcer distress or pain could be prevented by adequate treatment prior to the expected episodes.

If the patient's co-operation and understanding of the entire problem are good he soon perceives that, contrary to the layman's usual notion of ulcer treatment, the diet is not the principal means of treatment. Almost any physician who has had experience with ulcer patients will admit that the nervous factor is the dominant causative factor, but almost all of these same physicians feel rather hopeless when the job of applying this knowledge in the treatment of ulcer confronts them. They fall into the same pitfall which traps the



patient. They rely on diet and if that fails, as it often does when applied automatically, they immediately feel the ulcer is intractable and urge surgical treatment. The relative unimportance of the diet in the treatment of many ulcers is shown in the fact that such an ulcer may cause severe symptoms which remain unchanged in spite of vigorous measures until rapid clearing of some nervous factor leads to prompt alleviation of the symptoms of ulcer. In all probability the poor hope offered in statistical reports of healing of duodenal ulcers is the direct results of the inability of the physician to impress the patient sufficiently with the problem before him. It is not necessary to psychoanalyse the patient to treat the nervous factors. It is necessary to teach the patient to know himself, his weaknesses and his nervous characteristics and to realize their effect on his ulcer. This understanding of his own reactions is most important, and the intelligent application of frequent feedings permitted thereby merely serves to counteract the effect of a wide variety of factors on his weak spot, his duodenum.

From the start the patient should realize that his ulcer is an individual problem and that he has to help in establishing the basis for the treatment. He should not feel that ulcer is a condition about which he has to feel fatalistic and hopeless. Once he is aware of his function as a detective in finding the various features of his personality, work or environment which are acting unfavourably on his ulcer he usually contributes many essential points of which he has been aware. Cure of the ulcer is dependent on the patient's protection of himself from himself, in other words. Diet and antacids used in an intelligent fashion in order to prevent distress for one to two years can probably be considered to have rendered the ulcer quiescent. The evidence of the roentgenoscopic examination is of fully moderate value in deciding about healing of the ulcer. If all the evidence after two years indicates satisfactory progress, however, the patient may consider himself in the third stage of treatment, which involves prevention of further ulceration.

In the medical treatment of subacute duodenal ulcer it is necessary to insist on more intensive and more persistent care. The diet is liberalized more slowly, more rest is advised and, in addition to the faithful use of feedings of milk between meals, administration of antacids before and after meals is continued for many months and sedatives, as well as antispasmodics, are prescribed for use during the first month or two of treatment after hospitalization.

**Prevention of recurrence.**—After the duodenal ulcer is considered healed, the patient must understand several aspects of the problem if he is to prevent future recurrences.

In the first place, his previous self analysis has shown him the ease with which his periods of sustained nervous tension, anger, worry, anxiety, excess responsibility or work may lead to acute flare-up of his ulcer. He may have learned the wisdom of avoiding such episodes. However, not every one is able to change one's life enough to avoid such strains all the time. If periods of strain cannot all be avoided, sufficient insight may be developed so that the patient can recognize the strains which are dangerous and prevent harm to himself by intelligent use of frequent feedings, antacids and sedatives during the period of strain.

In the second place, the patient must realize the danger of returning to any of his old habits which are likely to be irritating to his ulcer. He must stay away from alcoholic beverages, tobacco in all forms and the various species, condiments and relishes which are so notoriously upsetting. Furthermore, he should make the taking of milk or milk and cream at 10 a.m., at 3-30 p.m. and at bedtime a habit which should last the rest of his life.

The fact that treatment has been successful enough so that the patient can liberalize his programme and rely on his knowledge and judgment of his own ulcer to prevent further trouble serves to give him a sense of confidence and hope for the future.

## Aqueous-Base Yellow Fever Vaccine

By M. V. HARGETT

H. W. BURRUSS

and

ANTHONY DONOVAN

(Abstracted from *Public Health Reports*, Vol. LVIII, 26th March, 1943, p. 505)

The preparation of aqueous-base living yellow fever vaccine was undertaken by the United States Public Health Service in 1941. This vaccine is an aqueous extract of 10- to 11-day-old chick embryos infected with the attenuated 17 D strain of yellow fever virus. It differs from the 17 D serum-base vaccine extensively used in recent years in that it contains 75 per cent rather than 10 to 40 per cent, embryo extract and no serum diluent. The extract is preserved by desiccation under high vacuum from the frozen state, with storage at subfreezing temperatures in an atmosphere of dry nitrogen. For administration the dried preparation is rehydrated and diluted 1:10 with physiological saline, with each recipient receiving 0.5 ml. subcutaneously.

The increased virus content of the aqueous product as contrasted with the serum-containing preparation insures that a greater quantity of virus is inoculated per individual vaccinated. This favours host immunization.

In excess of 600,000 doses of the aqueous type vaccine have been released to date for general use without encountering unfavourable reactions. Of 28 individuals studied, all possessed specific virus neutralizing bodies several weeks following vaccination.

Danger of vaccine contamination by serum containing pathogenic agents is eliminated.

## Clinical Value of Blood Sedimentation Rate (With a Plea for the Adoption of a Standardized and Simple Technique)

By E. OBERMER, M.D.

(From the *Practitioner*, Vol. CLI, July 1943, p. 43)

THE test discussed in this article has been in use ever since 1918. The number of determinations carried out all over the world has certainly run into millions. There is an extensive literature on the subject, in many languages. From the clinical point of view, the value of most of this literature is, however, limited, and in many instances nullified by the fact that the figures given, even when they are comparable among themselves, have not been correlated with a sufficient number of other blood findings, or with sufficient clinical data, to allow of accurate interpretation.

During the last few months, there has been a spate of letters to the medical press on this subject. Most of the writers disagree, and almost all seem confused, as to the best method to use the value of and the limitations of the test.

I have carried out more than 20,000 determinations since 1925. In each case the determinations have been correlated with the clinical picture, blood counts, as well as chemical and physico-chemical blood findings. As these data have been collected from all types of cases, covering the widest possible range of conditions, it may be useful to attempt a survey of the following:—

(1) Technique: the theoretical and practical requirements of an ideal method of determining the sedimentation rate, with a detailed description of a simple and universally applicable method.

(2) What the test means: what factors cause variations in the rate.

(3) The diagnostic value of pathological variations.

(4) Limitations of the method, and conditions which invalidate the test.



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## TECHNIQUE

After lengthy trials, a modification of Balachowsky's (1925) method was adopted. Although this method was not published until 1935, it has been in daily use since 1926. In practice it has fulfilled the following requirements, which are generally agreed upon:—

(1) The test should be simple and rapid of performance, and as reliable in the hands of the general practitioner at the bedside, as in the hands of the trained technician in the laboratory.

(2) To avoid fallacies due to capillary attraction, the bore of the tube used should not be less than 2 mm.

(3) The column of blood should be neither too short nor too long.

(4) Errors due to variations in temperature should be minimized. It is generally agreed that the rate is diminished to a variable extent by the lowering of temperature, and this cannot be corrected by calculation or a correction factor.

(5) The tube should be kept in a vertical position throughout the test.

(6) Dilution of the blood by anti-coagulant must be reduced to a minimum.

(7) The amount of blood used should be as small as possible.

The proposed technique has three further advantages over other methods in current use:—

(a) It involves a minimum of physical disturbance of the blood. There is no aspiration into a syringe, no shaking or mixing, no rapid cooling. As the sedimentation rate is the expression of a delicate physico-chemical equilibrium of the blood *in vivo*, all these factors may mitigate against accuracy.

(b) The three readings suggested, *i.e.* at a quarter, half, and one hour, make the method more sensitive than any other, thus giving a wider range of physiological, physio-pathological and pathological variations.

(c) Variations in red cell count can be corrected by a simple calculation.

*Details of the method. Apparatus required:—*(1) A Francke's lancet, or any other instrument for making a deep prick in the pulp of the finger.

(2) Lengths of capillary tubing—10.4 cm. by 2 mm. bore.

(3) Plasticine.

(4) Thick-walled test tube (6-inch by  $\frac{1}{2}$ -inch) with cork.

(5) Pocket ruler, in metal or celluloid, 10 cm. long, graduated in millimetres.

(6) A leather fountain-pen holder with safety pin to attach to waistcoat pocket to hold test-tube. When the test is to be carried out in a laboratory equipped with 37°F. incubator, the holder can be dispensed with.

(7) A small bottle of saturated solution of sodium oxalate.

*Procedure.*—It is important that the capillary tubes, the test-tube, oxalate solution and plasticine should be kept at body temperature. They should therefore be kept in an incubator or carried in the waistcoat pocket.

The patient's hand should be immersed in very hot water, long enough to turn it lobstered. While the patient is warming his hand, a capillary tube is dipped in the oxalate solution, and allowed to fill by capillary attraction. It is then laid on a bench or bedside table, together with a ball of plasticine about 10 mm. in diameter. The patient is told to dry the hand and place it in the supine position on a towel.

A deep prick is then made in the pulp of a finger. Most of the oxalate is shaken out of the tube, leaving a column, at the bottom end, of exactly 4 mm. (measured by ruler). The finger is gently squeezed with the left hand, so that a large drop of blood wells out of the pulp. The oxalated end of the capillary tube is dipped into the blood at an angle of about 60°. The blood will then flow up, partly mixing with and partly pushing the oxalate in front of it. When the column of blood has been pushed half-way up, the capillary tube should be reversed, the column of blood

run to the other end, and this end inserted into the drop of blood until the whole length of the tube is filled.

The ball of plasticine is then held in the left hand, the blood-filled tube, horizontally, in the right hand, and the left end of the tube is inserted into the plasticine for a depth of 4 mm. This can be verified by measuring the length of the projecting tube; it should measure exactly 10 cm.

The tube is then placed vertically in the incubator, or dropped into the test-tube in the waistcoat pocket. Readings of the supernatant plasma are taken at the end of fifteen, thirty and sixty minutes.

The upper limits of normality by this method are:—

15 minutes	..	up to 0.4 cm. (4 mm.)
30 "	..	" 1.0 cm. (10 mm.)
60 "	..	" 2.5 cm. (25 mm.)

When red blood cell figures are available, no correction need be made unless the count is below 4 millions or over 5½ millions. Above or below these limits, the reading should be multiplied by the factor *R.B.C.* in millions.

## WHAT THE TEST MEANS

This is not the place to discuss the highly technical factors involved in the mechanism of erythrocyte sedimentation; even experts do not agree on this subject. Readers are referred to Balachowsky (1925) for intrinsic red cell factors, to Bendien and Snapper (1931) for the plasma protein factor (the authors prove that there is a direct correlation between fibrinogen content and sedimentation rate) and to Rossier (1927) for physico-chemical details. The last named author showed a parallelism between curves of sedimentation rate and iso-electric points of the plasma. The following facts, however, are well established:—

(a) The sedimentation rate is surprisingly constant for the individual under physiological conditions.

(b) *In vivo*, or at body temperature, the normal equilibrium between red blood cells and plasma is ruptured by a large number of physiological as well as pathological phenomena. Thus the absorption into the blood stream of minute quantities of foreign protein, colloidal metals and a number of other substances is sufficient to increase the sedimentation rate to a significant extent.

(c) Extravasated blood from a simple bruise or from the uterine cavity during menstruation, placental proteins, and even absorption of cells, destroyed as part of the ordinary wear and tear of the tissues (when ketabolism is accelerated) may influence the rate to an even greater degree. It is therefore important for the clinician to realize that the results of this test must be interpreted with the greatest reserve. From the diagnostic point of view, abnormal figures, *i.e.* an increased rate, have relatively little value unless correlated with many other data. More reliance, however, may be placed on normal figures. Even so, it must be stressed that normal figures mean, simply, that no absorption of abnormal products is taking place.

It is reasonably safe to assume that the presence of an inflammatory process is incompatible with sedimentation rate figures which are within normal limits. There are, however, rare exceptions to this rule. A few people, for reasons which are not yet understood, have an extraordinarily slow sedimentation rate.

In one case in my series (a young man of thirty), serial determinations were done over a period of two to three years. In health, his rate never varied, *i.e.* 0.0 at fifteen minutes, 0.2 at thirty minutes, 0.5 at sixty minutes. Throughout an acute pyrexial attack of tonsillitis, during which daily determinations were made, the rate remained within normal limits.

The rate is also abnormally slow in the presence of polycythemia, at high altitudes and in persons of a plethoric habitus.

Finally, the clinician should remember that increased plasma volume, due to anaemia, causes an increased rate of sedimentation. When a red blood cell count is possible, a correction can be made. In its absence, if the clinician suspects anaemia, he cannot attach any importance to an increased rate. For further details on this point readers are referred to Walton (1933) and Schuster (1938).

#### DIAGNOSTIC VALUE OF PATHOLOGICAL VARIATIONS

**Explanatory.**—From what has been said it will be seen that many pathological processes within the body cause a marked increase in the sedimentation rate, owing to the fact that normal cells, when damaged, function as foreign protein. An increased rate may therefore be caused by blood extravasated through injury or operative interference, by transudates or exudates, by autolytic or necrotic tissue changes, as in malignant neoplasms, syphilitic gummas; and also by caseation and fibrinoplastic changes.

It is also true that the rate is increased when the body is reacting to an inflammatory process. The degree of increase tends to be proportional to the severity of the infection. Such an increase is almost certainly due to the inflammatory reaction or, rather, the absorption of the products of such a reaction. Thus, the rate is very rapid in osteomyelitis and in acute furunculosis, but is not increased in the presence of a 'cold' abscess. It may be assumed that the latter is due to the fact that the pus in a 'cold' abscess is completely 'walled round', and that there is no systemic absorption from the pus sac.

By the same rationale, it is legitimate to use the sedimentation figures as a rough estimate of the degree of systemic toxic absorption in a number of conditions. Thus, if the rate is normal when dental skiagrams show an apical abscess, the clinicians may be justified in asking the dentist to spare the tooth; the abscess is probably 'walled round' and is not doing the patient any harm. It is, as yet, a moot point whether or not the absorption of bacterial toxins alone can cause an increase in the rate.

**In miscellaneous conditions.** (a) *The 'abdominal' case.*—A negative test at the bedside in an acute abdomen may help the clinician to differentiate between simple colic and appendicitis or other inflammatory process within the abdomen. The same applies to acidotic vomiting in children and the differentiation of an allergic colitis from an infective one.

(b) *Functional cases.*—An increased rate may be found on examining individuals complaining of symptoms without any detectable physical signs. In such cases it is often justifiable to incriminate focal sepsis.

(c) *Rheumatism.*—This test can be of some small assistance in the blind groupings through this diagnostic 'no man's land', but it should never be used as a 'compass'. The factors involved are far too complicated to permit anyone, however skilled, to use sedimentation figures as a guide to prognosis or treatment. In well-defined pathological joint states, such as rheumatoid arthritis, that rate is invariably increased, but variations in the clinical condition are a more reliable guide to progress than the sedimentation rate. When there is nerve or muscle pain, a negative test is of some value, as the clinician can then, tentatively, exclude active focal sepsis.

**Acute and subacute infections.**—In mild infections, such as coryza, an increase in the sedimentation rate is usually proportional to the degree of systemic disturbance. If tracheitis or bronchitis supervene, the rate of sedimentation is often a better guide than the temperature curve. Similarly, in the subacute phase of influenza, otitis media, pelvic or urinary tract infections, an increase, instead of a decrease, in the rate may put the clinician on his guard against complications. A maximum increase in the rate is found (a) during the acute phase of the common fevers, in particular scarlet fever, in which the fibrinogen content of the blood is very high, and (b) in lobar pneumonia, owing to the double effect of toxic absorption and resorption of the pulmonary exudate.

**Chronic infections.**—Enough has already been said to show that variations in so sensitive a test should never be used as a reliable guide to prognosis during complex, long-drawn-out disease processes. This applies particularly to a protean disease, such as *pulmonary tuberculosis*. It is true, however, that the test has been used, or rather misused, in this disease more than in any other single clinical condition. Variations in the sedimentation rate and in 'sediment index' (an ingenious mathematical abstraction—unfortunately worshipped by its devotees as an infallible prognostic deity) have been interpreted with the most unjustifiable dogmatism. As secondary infection is extremely common in chronic pulmonary tuberculosis, and as autolytic and reparative changes in the lung continue even in a quiescent or arrested case, the accurate interpretation of sedimentation changes in tuberculosis is well nigh impossible. In fact, it may be said that an increased rate of sedimentation in pulmonary tuberculosis can be considered of clinical significance only when it is correlated with all the clinical and radiological data, and with simultaneous determinations of plasma protein content (by an accurate chemical method), plasma viscosity refractive index of the plasma (permitting a rough estimate of the albumin globulin ratio) and a complete blood count, including a Schilling or Arneith differentiation of the polymorphonuclear cells. As facilities for such a complete investigation are rarely available in sanatorium or dispensary practice, the test is of doubtful utility in this condition.

#### LIMITATIONS AND CONTRAINDICATIONS

The test cannot be relied upon in the following circumstances:—

(1) *Infancy.*—During the first few months of life, the red blood cells do not sediment; no satisfactory explanation has as yet been put forward.

(2) *During menstruation.*—Some women consistently show an increase in the rate during the flow. In others the rate remains normal. Here again, no explanation has been put forward. It is to be hoped that the mechanism of this phenomenon will be worked out, as it may throw light on several obscure pelvic problems. From a practical point of view, however, it is wiser not to perform the test on women during the menses.

(3) *Pregnancy.*—From about the twelfth week of pregnancy to the fourth week post-partum, the rate is invariably increased.

(4) *After accidental or operative trauma.*—Until healing or cicatrization has occurred.

(5) *Hypodermic treatment.*—Subcutaneous or intramuscular injections of vaccines, peptone, casein, or other foreign proteins, colloidal metals and auto-haemotherapy.

#### CONCLUSIONS

The sedimentation rate of the blood reflects static phases of a delicate and unstable equilibrium. This equilibrium is destroyed or disturbed by the absorption into the blood stream of a number of substances of which inflammatory products are only one. So sensitive a test is undoubtedly capable of yielding information of the greatest value to the clinician. However, much of this information cannot yet be interpreted with accuracy, because different workers have used different methods and have not adequately correlated the sedimentation figures with other blood findings and clinical data. The way forward to a clearer understanding of the value of this test is twofold:—

(1) Through the routine use of a standardized test by a large number of practitioners in their surgeries and at the bedside.

(2) The wider use of laboratory facilities in hospitals, sanatoria and research institutes, for more comprehensive blood work, including a determination of the sedimentation rate by the same standardized method.

Only thus can a new literature on the sedimentation rate, of practical as well as theoretical value, be estab-

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lished to replace the present confusing record of dissociated and uncorrelated data.

#### SUMMARY

(1) The theoretical and practical requirements of an ideal method for determining the blood sedimentation rate are given.

(2) A simple method for estimating the sedimentation rate in the laboratory or at the bedside is described.

(3) The mechanism of sedimentation is discussed.

(4) An explanation is given for variations of the rate in physiological and pathological conditions.

(5) The use of the test in various conditions, and inflammatory processes, is subjected to a critical review.

(6) Stress is laid on the value of normal figures (a negative test), and upon the necessity for extreme caution in interpreting abnormal figures.

(7) A list is given of the conditions which contraindicate the use of the test.

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### Some Therapeutic Fallacies

By J. W. LINNELL

and

W. A. R. THOMSON

(From the *British Medical Journal*, ii, 6th November, 1943, p. 572)

A FEW years ago one of us had occasion to give a clinical lecture in a London hospital to a number of general practitioners. In it he happened to question the value of certain generally accepted forms of therapy, to be hotly attacked by a section of his hearers on the score that he was taking away their 'treatment'. It was in vain he protested that if this could be proved to be valueless it should be discarded. They were not to be pacified. Shortly afterwards he had a similar experience in the Provinces. This paper owes its origin to these two incidents. It is not to be expected that all our conclusions will be accepted by all our readers. If they succeed in evoking a critical spirit—now alas! sadly lacking—in regard to present-day methods of treatment, we shall be content.

#### ESSENTIAL HYPERTENSION

The number of men and women in middle and late middle life who 'suffer' from this condition is enormous. The number who are living full and vigorous lives in blissful ignorance of the fact that their blood pressures are abnormally high is immeasurably greater. Of those in the first category few would have any symptoms referable to the condition if they had not been informed by their doctors that they were its victims. Uncomplicated high blood pressure gives rise to no symptoms of itself in the large majority of patients; few without knowledge of its presence complain of dizziness, a sense of fullness in the head, occipital headaches, and any others of the list of symptoms ascribed to it in textbooks of medicine. Such symptoms are nearly always due to an anxiety state largely dependent on knowledge of the height of their blood pressure.

Before criticizing the usual treatment of hypertension it is well to remember that its cause is quite unknown, even if innumerable theories regarding it have been advanced at one time or another. In spite of common medical belief to the contrary, infections, whether general or local, auto-intoxication derived from the bowel, prolonged physical strain, and a high protein diet have, so far as is known, nothing to do with it. Nervous strain may raise it temporarily; there is no evidence that it can produce it. Endocrine disturbances are easy to blame; they are harder to incriminate.

In view of these facts treatment must be unsatisfactory. It can be said at once that therapeutically we are powerless to reduce blood pressure save temporarily. Nevertheless, prolonged rest in bed, regular purgation, repeated venesections, diets of many descriptions, all manner of baths, scores of drugs and organic extracts, high-frequency currents, diathermy, and we know not what else are constantly being used by the overactive therapist. The public also 'like treatment' and is willing to pay for it. In the present state of our knowledge is it not more logical for us to approach the question of treatment as philosophers? A patient who has been told that he has a high blood pressure often lives in constant dread of a 'stroke'. Then why tell him when we discover it? If he has been told already, why not reassure him by telling him of people with blood pressure as high as or higher than his who are living full and active lives; that many of them will reach the allotted span; and that if we could bring down his blood pressure the chances are that he would feel the worse for it? In the case of the relatives of course, the position is rather different, and they should be informed that the expectation of life is not so good as in an individual with normal or low blood pressure. So long as there are no complications the patient should not be allowed to consider himself an invalid; on the contrary, he should be urged to keep up his interests, though on general grounds he should be advised to avoid overstrain, both physical and mental. He should be encouraged to take moderate outdoor exercise: golf played in leisurely manner is—or, alas! was—the game *par excellence* for hypertensive patients. Often they sleep well. When there is insomnia sleep should be ensured by a nightly dose of a sedative, but no one should be initiated into the habit unnecessarily. He should be allowed an ordinary mixed diet, unless perchance he be obese, when his weight should, if possible, be brought down gradually to reasonable proportions by dieting. This last is a most important measure, as, for one thing, there seems to be some connection between obesity and hypertension; for another, it seems illogical to allow an already overworked left ventricle to be subjected to a further strain which is avoidable; and, for yet another, the raised diaphragm and its small range of movement present in obese people can only increase the heart's handicap. A hypertensive patient who has brought himself to submit to the loss of superfluous flesh is greatly gratified, as a rule, by the results of his abstinence.

#### HYPOTENSION

On recent years there has been an increasing tendency to diagnose a condition known as 'low blood pressure'. In consequence a new sword of Damocles has been hung over the heads of numbers of healthy people. A doctor, unable to find any organic cause for a patient's complaints, discovers in the course of his examination that he has a systolic blood pressure of something in the neighbourhood of 100 mm. Hg. He immediately fastens on this, with the result that a new invalid is created, to become almost inevitably the victim of polyvalent therapy.

Except in a very small and limited group of conditions such as shock, severe hæmorrhage, coronary thrombosis, Addison's disease, and a severe infection such as influenza, hypotension is of no clinical significance. Our practice is, when we find a middle-aged

man with such a blood pressure as we have mentioned and for which there is no apparent cause, to congratulate him upon the state of it. Apart from aught else, such a man is almost certainly immune to hypertension.

#### ARTERIOSCLEROSIS

For this there is no known treatment. Yet how much honest endeavour is wasted in striving to stay its progress and restore its ravages! Why pretend to achieve the impossible? Surely it is better to accept the inevitable. No useful purpose, however, is served by telling a patient that he has arteriosclerosis. That much can be done to help him and his relatives by advice and by treatment of various symptoms as they arise is certain. Nevertheless, the chances are that he will profit most by encouragement.

#### ANGINA PECTORIS

The number of drugs used to reduce the frequency of attacks of angina pectoris should alone make one suspicious of the efficacy of any of them. Evans and Hoyle (1933, 1934) in a fine piece of work tested a host of them—sodium nitrite, mannitol hexanitrate, erythrol tetranitrate, potassium iodide, luminal, chloral, morphine, papaverine, phenacetin, diuretin, euphyllin, belladonna, digitalis, lacarnol, and harmol—to find that none of them acted better than the placebo they used as a control. And yet there must be few of the thousands of victims of angina pectoris in this country who are not taking at least one of them regularly on the advice of their doctors.

Nitrites, particularly in the form of freshly prepared glyceryl tetranitrate tablets, dissolved rapidly in the mouth before being swallowed are of inestimable value not only in cutting short individual attacks but also in preventing them if they are taken immediately before exposure to such conditions as are known by experience to be likely to induce them. So transitory is their effect, however, that to give them, say, three times a day—as is often done—to prevent attacks is even less reasonable than to inject adrenaline three times a day to prevent attacks of asthma.

#### CARDIAC BRUITS: SIMPLE TACHYCARDIA

It would seem that to many practitioners the mere presence of a bruit is enough to warrant the administration of digitalis. The single indication for digitalis is heart failure in some degree, and this whether the bruit be or be not of organic origin.

Again, the mere presence of tachycardia seems still to many practitioners an indication for digitalis. It has no effect in simple tachycardia due to nervous, toxic (including thyrotoxic), and anæmic states. It is heart failure and not tachycardia which is the indication for digitalis.

#### PAROXYSMAL TACHYCARDIA

An attack of paroxysmal tachycardia often arouses needless anxiety in patient and doctor alike, and recourse is straightway had to a variety of drugs, including inevitably digitalis. The first thing is, naturally, to make an accurate diagnosis, for it is necessary to exclude an unusual degree of simple tachycardia, paroxysmal auricular fibrillation, and paroxysmal auricular flutter. An electrocardiogram taken during an attack is of great value, though not always essential. Paroxysms differ in origin and type and affect both healthy and diseased hearts. The treatment varies from type to type, and the prognosis from patient to patient, but there are a few valuable rules to keep in mind as regards both.

Sometimes the tachycardia is ventricular in origin. Here the prognosis is usually grave, as in the large majority of patients serious myocardial disease is present; most cases, indeed, follow an attack of coronary thrombosis. It is then vital to stop the paroxysm as soon as possible. Digitalis, however given, is almost certainly ineffective and in large doses may be positively harmful, whereas quinidine sulphate, whether given by mouth or intravenously, may produce some

of the most dramatically beneficial results in medicine. Far more commonly the tachycardia is supraventricular in origin, either auricular or nodal. Here the prognosis is usually excellent, as in the large majority of cases the myocardium is healthy—it is, indeed, practically only in cases of very diminished cardiac reserve, whatever the cause, that the prognosis is doubtful. Paul White (1937) goes so far as to say that the condition is 'usually unimportant'. Unless the life of the patient is crippled through the frequency or the length of attacks, or the reserve of the heart is known to be already small, active treatment is unnecessary. It is generally advisable for the patient to rest during an attack; otherwise, little is needed save strong reassurance as to its innocence. Moreover, a small percentage of patients can themselves stop an attack by pressing on the carotid sinus in the neck, holding the breath, inducing retching, adopting a certain posture, and so on. If it is deemed advisable or necessary to stop an attack on account of its long continuance a subcutaneous injection of acetyl-beta-methylcholine chloride is the procedure most likely to be successful, though it is one never to be hastily adopted since its effects in other ways may be alarming. Digitalis neither stops paroxysms nor diminishes their incidence. Quinidine sulphate is reputed to do with occasionally, although this is not our experience.

As a toxic goitre is sometimes responsible for the disorder it is always wise to exclude its presence, since a subtotal thyroidectomy in such a case may be the means of dispensing with all other kinds of treatment.

#### PAROXYSMAL AURICULAR FIBRILLATION

Marvellous as is the effect of digitalis in most cases of established auricular fibrillation, it will not stop individual attacks of paroxysmal auricular fibrillation, nor is there any satisfactory evidence that its regular administration prevents such attacks. In themselves these are—contrary to general belief—usually surprisingly harmless, and there is, as a rule, no urgency to endeavour to stop one, as it may easily and spontaneously cease after a short time. If, however, it persists hour after hour to the great discomfort of the patient, or if the cardiac reserve is known to be small, and in any case if signs of congestive failure appear, it can usually be stopped by the oral administration of quinine sulphate at frequent intervals. As one of the most fruitful causes of paroxysmal auricular fibrillation is thyrotoxicosis, and a subtotal thyroidectomy generally results in a complete cessation of attacks, in every case a goitre should be diligently searched for—even if mitral stenosis is present.

#### SHOCK

This is a result of vasomotor and not cardiac failure. Drugs such as digitalis and strophanthin, which are often administered, have therefore no place in its treatment. It should be remembered too, that with a reduced volume of blood reaching the heart it is necessary for it to beat rapidly to maintain the circulation.

#### BLEEDING

Calcium is widely used in the treatment of purpura, menorrhagia, hæmoptysis, epistaxis, post-operative hæmorrhage and hæmophilia. It is also often given before operation as a prophylactic against hæmorrhage. Yet, according to Hunter (1938), there is no pharmacological evidence that it either increases the coagulability of the blood or shortens the bleeding time. In his opinion there is no justification for its use in such conditions as we have mentioned; and, as regards its use before operation, it is only of value in cases of obstructive jaundice, in which probably part of the existing blood calcium has become bound to the bile pigment and is thus unavailable for the process of coagulation. Even in these cases administration of vitamin K is more important.

#### CHILBLAINS

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Yet there are no sure grounds for its use. In all these conditions the serum calcium is normal.

#### ANÆMIA

Tens of thousands of people are treated for anæmia who are not anæmic. A clinical diagnosis of anæmia is apt to be fallacious. In the examination of any patient in whom anæmia is suspected an estimation of the hæmoglobin should never be omitted. If anæmia is found to be present every endeavour should be made to discover its cause. This may be revealed in the course of a thorough clinical examination. Often a full examination of the blood is not only advisable but necessary.

Most cases of anæmia with a low colour index are benefited by iron if effective preparations are used in adequate dosage. It is, however, often discarded as useless after trial in perfectly proper cases simply because the dosage has been inadequate. In this connection we consider the recent fashionable craze for giving iron by injection deplorable. According to Witts (1930-31) the majority of ampoules of iron on sale contain infinitesimal amounts of the metal and are ineffective; the potent preparations cause much pain and occasionally iron poisoning. Vaughan's (1932) dictum that intravenous, intramuscular, and all proprietary preparations of iron are as useless as they are expensive is practically true.

Again liver is not a panacea for every type of anæmia. It is, with rare exceptions, only of value in the treatment of pernicious anæmia and other megalocytic anæmias. As regards the method of its administration, on all grounds—cost, comfort, convenience, and effectiveness—parenteral therapy is infinitely preferable to oral; indeed, the latter method should now be considered archaic save in a few cases. Much has been written on the necessity for giving dilute hydrochloric acid as well as liver. It seldom relieves any accompanying indigestion; it has no effect on the anæmia.

Finally, there is no evidence that arsenic is of any value in the treatment of either microcytic or megalocytic anæmia.

#### TOXIC GOITRE

The truth of Joll's (1932) statement that subtotal thyroidectomy is 'the method which most rapidly, most certainly, and most safely restores the patient to a state of economic efficiency and involves least likelihood of danger of relapse' is now firmly established. Iodine does not cure. This truth cannot be stressed too strongly. In most cases, for reasons not yet understood, it ameliorates the signs and symptoms, but only temporarily. Its administration for a short period before and immediately after operation has contributed not a little towards the extraordinary safety which now attends subtotal thyroidectomy when conducted by a team of experts. In our opinion its use should be restricted to these periods. The common practice of giving it for months and even years on end in the belief that it cures is strongly to be condemned. Thereby operation is often postponed till cardiac complications, extreme emaciation or a psychosis supervenes.

#### THE COMMON COLD AND INFLUENZA

The clamant demand of the layman for a cure of these, the bane of his life, would appear to have had such an undesirable effect on our profession that we feel it our duty to insist on the usefulness of preventive inoculation. In spite of the many large-scale investigations that have been carried out, not one of which has shown that any benefit accrues from such treatment, uncritical impressions still hold the field, and numberless patients are subjected year after year to prophylactic courses of vaccines.

Another point: sulphonamide compounds have no action on filter-passing viruses. It is unwise, therefore, to give them to patients suffering from uncomplicated colds and influenza. Moreover, to quote Beaumont and Dodds (1941), the prophylactic

administration of small doses of sulphanilamide against various types of infection, such as sore throats or colds, is useless.

#### BRONCHITIS

A diagnosis of bronchitis, whether acute or chronic, means almost invariably the prescription of an expectorant. The number of gullions of expectorant mixtures used in this country alone in any one year is enormous. That their action is beneficial is taken for granted. Yet it is doubtful if they do not do more harm than good. It seems not only a clumsy but a harmful procedure to try to increase bronchial secretion by irritating the vagal nerve endings in the delicate mucous membrane of the stomach through the administration of sub-nauseating doses of emetics. Nevertheless, this is how such expectorants as ipecacuanha, ammonium carbonate, and squills act—if they do act effectively when used in pharmacopœial doses, which is not certain. The chances are that they do little more than cause gastritis. It may be said that this accusation cannot be brought against the iodides. Their action, however, has been found to be very variable, and is probably dependent on the sensitiveness of the individual patient to iodine. What is urgently needed, of course, is a complete reconsideration of the whole subject of expectorants. Unfortunately, as Clark (1937) says, the pharmacology of cough has scarcely advanced at all in the last half-century. We, for our part, have practically given up expectorants in the treatment of bronchitis. In acute bronchitis—a condition which tends to spontaneous cure—we rely chiefly on rest in bed, an abundance of hot drinks, steam inhalations, and sedatives to control an irritating cough; in chronic bronchitis, on general measures as they affect physical condition, climate, environment, occupation, etc., and, since chronic bronchitis of any standing inevitably connotes bronchiectasis, we advise such patients as seem capable of it to practise postural drainage every morning and at intervals during the day.

This can be achieved very simply by a patient stretching himself across a bed or couch with the trunk hanging steeply over the side and coughing till no more sputum is produced.

#### LOBAR PNEUMONIA: BRONCHOPNEUMONIA

In spite of the amazing success of sulphapyridine (M&B 693) and allied preparations in this disease there is still need for the well-established non-specific methods of treatment: measures to achieve rest and sleep, good nursing, a sufficiency of fluids, and oxygen. Special attention has always been directed towards the heart. Most doctors seem to visualize a heart poisoned by infection gradually dilating as it becomes flabbier till in the end it fails. Yet seldom, even in fatal cases, are the classical signs of congestive heart failure seen. Moreover, in a radiological study of 119 hearts in pneumonia by Davies, Hodgson, and Whitby (1935) definite enlargement was witnessed in no more than three. It is not cardiac failure which is to be feared; it is peripheral circulatory failure. This is due to loss of contractility of the muscular coat of the peripheral arterioles, with consequent stasis of the blood in the capillaries.

If this be the case, the uselessness of so-called 'heart tonics' is manifest, even if they can ever be proved to have any stimulating effect on the myocardium. Certainly alcohol, whatever its value as a food or a sedative, has no such action, nor have strychnine and camphor, while strychnine does not appear to exert any effect on the poisoned peripheral vessels. Digitalis—in popular medical opinion the most potent of all 'heart tonics'—is, after all, a poison, and its beneficial effects must be very convincing to warrant the further poisoning of an already poisoned organ. As a matter of fact, its effect in lobar pneumonia has been carefully investigated by many workers, among whom Wyckoff, DuBois and Woodruff (1930) concluded that its routine use was dangerous and in large doses increased the mortality; while Cohn and Lewis (1935)



in an analysis of 1,456 cases found that it did not influence the course of events. Whatever be the value of expectorants under any circumstances, they should logically have little place in the treatment of lobar pneumonia unless there is an associated bronchitis, for most of the exudate are absorbed and not expectorated.

All we have said about the heart, the circulation, heart tonics, etc., in lobar pneumonia holds also in broncho-pneumonia. The value of such preparations as sulphapyridine in the individual case is, however, much more a matter of trial and error. Success or failure probably depends on the extent to which the pneumococcus is responsible for the infection, and this is difficult to assess.

#### CONSTIPATION

Incredible quantities of purgatives are ordered daily by doctors, in most cases needlessly and in many harmfully. In the first place to treat roughly and ignorantly a marvellous piece of mechanism like the intestinal canal, with its delicate epithelium, its wonderful secretory and absorptive apparatus, and its beautifully balanced rhythmic movements, is little less than an outrage. There is an ingrained belief in doctors and patients alike that manifold evils will result if the bowels are not opened once at least every twenty-four hours. Yet as Gee insisted many years ago, this is not a natural law, and many people feel in better health when the bowels act once in every two or three days. There is little or no evidence to support the widely held opinion that auto-intoxication results from simple constipation: fæces are, after all, meant to dry in the distal colon, and toxic absorption is far more likely to derive from fluid fæces than from dry scybala. To quote Witts (1937): 'Apart from mechanical distension, a constipated stool exerts little more influence on the patient in the colon than in the bed-pan'. Again, in many people who complain of constipation the fæces arrive normally at the pelvic colon, but subsequent evacuation is not adequately performed owing to loss of the conditioned defæcation reflex, generally caused by continued neglect to respond at once to the call to stool. It is, however, in the constipation met with in acute infections that purgatives may be definitely dangerous. Here constipation is chiefly due to dehydration, and to dehydrate further an already dehydrated patient seems hardly logical. Once more, though there has been of late a change of mind on the part of most surgeons as regards the preparation of patients for operation, the practice of preliminary purgation in all cases still obtains in some quarters. To dehydrate deliberately before operation and to use all kinds of ingenious means to dehydrate immediately after would seem to be the acme of illogical thinking.

We ourselves have less and less recourse to purgatives with the years. Much can be done by stressing the harmlessness of constipation. 'The ill effects of constipation are almost entirely psychogenic and due to worry over disturbance of habit' (Witts, 1937), and anxiety about the action of the bowels is probably in itself a fruitful cause of constipation. Much, again, can be done by insistence on the necessity for cultivating a regular habit, diet, exercise, the provision of a low lavatory seat or the adoption of a squatting posture for defæcation, and the lubricant, liquid paraffin. There is seldom any urgency to open the bowels in acute infections under four or five days, and then this should be done by enemata and not by purgation. Enemata are almost certainly not used enough in the treatment of chronic constipation; a regular habit can often be regained by their daily use in constantly decreasing amounts.

Our thanks are due to Drs. John Parkinson, Donald Hunter, Hugh Dunlop, and Clifford Hoyle for their helpful criticism of various points we have tried to make in this very incomplete and discursive paper.

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## Reviews

**THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE: A UNIVERSITY OF TORONTO TEXT IN APPLIED PHYSIOLOGY.**—By C. H. Best, M.A., M.D., D.Sc. (Lond.), F.R.S., F.R.C.P. (Canada), and N. B. Taylor, M.D., F.R.S. (Canada), F.R.C.S. (Edn.), F.R.C.P. (Canada), M.R.C.S. (Eng.), L.R.C.P. (Lond.). Third Edition, 1943. Baillière, Tindall and Cox, London. Pp. xvi plus 1942. Illustrated. Price, 55s.

A VOLUME of 1800 pages on applied physiology is likely to frighten even the most enthusiastic reader, but once he gets down to it, he will be struck with its wealth of material and the mastery with which the subject-matter has been presented in this book. It is divided into nine sections, each dealing with a particular system of the body and packed with valuable 'up-to-date' information. The general plan of the book is to give details of physiology that have bearing on medical practice and to follow it with description of 'morbid physiology', indicating the principles underlying diseased states and how a knowledge of these principles may aid in diagnosis and treatment. Clear and comprehensive, to read it gives a feeling of satisfaction, arouses interest and reveals how physiology is intimately related to clinical medicine. The book is especially valuable to teachers of medicine and those working for higher examinations.

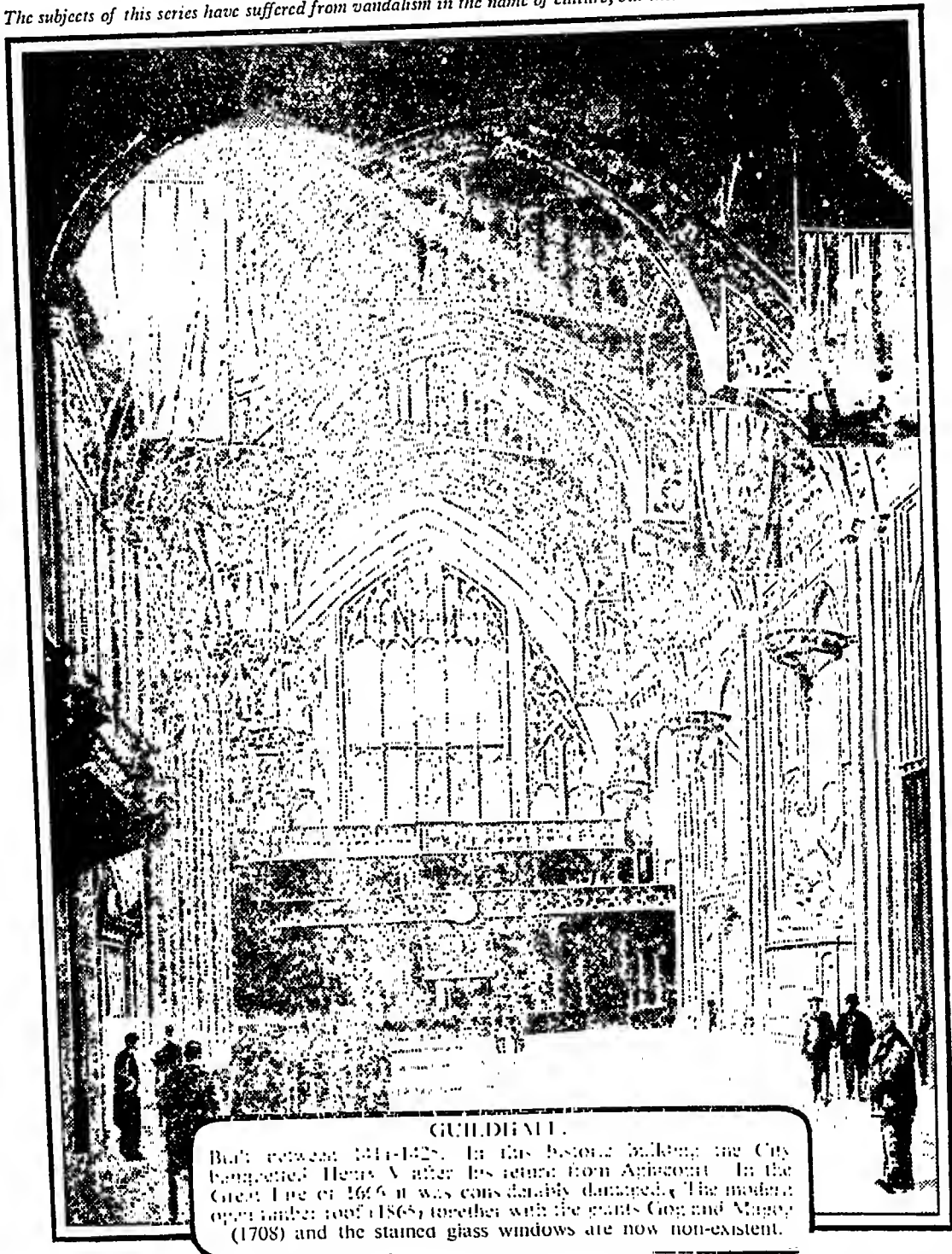
R. N. C.

**THE EPIDEMIOLOGY, PATHOLOGY AND DIAGNOSIS OF CHILD LEPROSY (BEING THE DR. ELIZABETH MATHAI ENDOWMENT LECTURES, 1942-43, DELIVERED AT THE MEDICAL COLLEGE, UNIVERSITY OF MADRAS).**—By R. G. Cochrane, M.D. (Glas.), M.R.C.P. (Lond.). Printed by the Superintendent, Government Press, Madras. 1943. Pp. 24

THESE three lectures by the Chief Medical Officer of the Lady Willingdon Leprosy Sanatorium stress the importance of child leprosy, stating that in many respects leprosy can be considered a child disease since the majority of patients in highly endemic areas contract the disease in childhood. The first section of the lecture discusses the epidemiology of leprosy, stressing the importance of three factors in the spread of leprosy: the type of leprosy, the age of a person exposed, and the type of contact. A study of cases seen at Saidapet indicates that the more serious forms of leprosy are acquired from the closer contact with the more infectious cases at an early age. The limited influence of diet in the causation of leprosy is stressed. Family susceptibility is considered not to be a major factor. The greater susceptibility of people of certain racial

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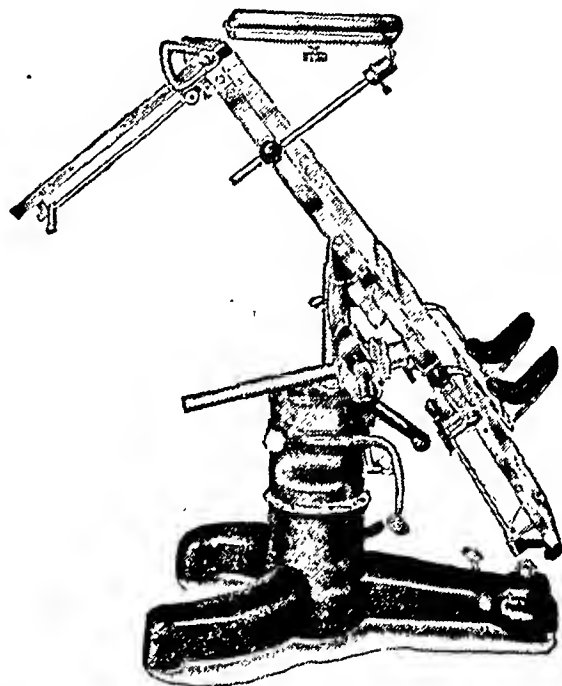
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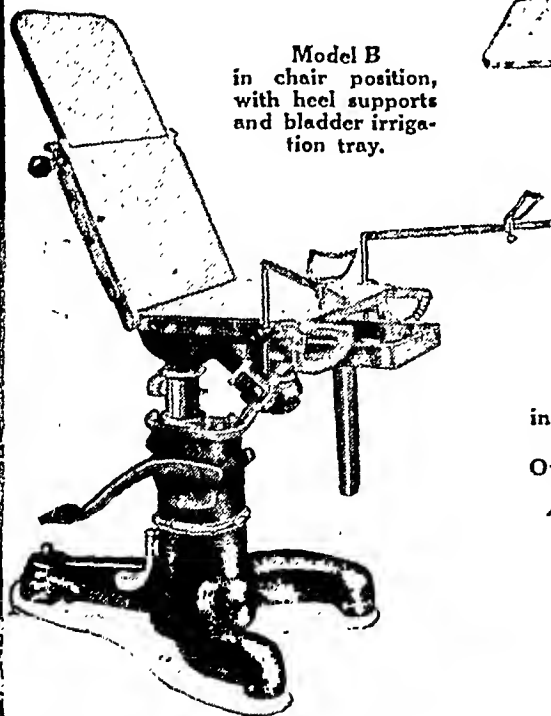
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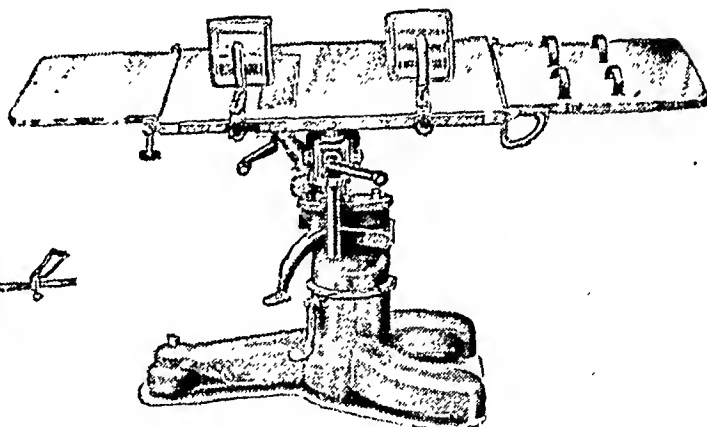


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groups and the higher incidence in males are briefly discussed.

The second lecture is headed 'Pathology of child leprosy' but it ranges over a wider field than is indicated by this title. In addition to pathology it discusses the self-healing nature of leprosy, the defence mechanism of the body against leprosy, the latent period, the initial lesions of leprosy, and also immunity in leprosy and immunological tests.

The third lecture deals with the diagnosis of child leprosy. The discussion is along generally accepted lines but many useful practical tips are given. The author makes a plea for the recognition of the special type of leprosy seen in 50 per cent of cases of leprosy in children in Saidapet. These lesions he calls 'incipient lesions' and he stresses the absence of the ordinary diagnostic signs of leprosy and the consequent difficulty in diagnosis and the relatively serious prognosis of these cases.

The author of these three lectures has made a special study of leprosy in children, and here he presents the main findings of his study of this important matter.

**TECHNICAL EDUCATION.**—By J. C. GHOSH, B.Sc. (Manchester). Second Edition. 1943. Published by P. K. Ghosh, School of Chemical Technology, Calcutta. Pp. xvi plus 316. Price, Rs. 3 (postage extra) or 5s. 6d. (postage free)

The book is an attempt to inspire Indian youths with a new conception of education and careers. It contains articles on technical education in general and on chemical and pharmaceutical education in particular, in which the author urges the developing of industries with the application of science and suggests measures for tackling the problem of middle-class unemployment. In the present edition some new matter has been added on education and industries.

R. N. C.

**THE INDIAN JOURNAL OF SURGERY.\*** Volume V, No. 4, December, 1943

A copy of this quarterly publication of the Association of Surgeons of India has reached us. It reprints some verses from 'Ashtanga Hridaya Chikitsa Sthana, Chapter II' describing stone in the bladder and discusses the ancient form of treatment for this condition. Other contents are as follows: an article by Menon, Reddy and Jacob on 'Primary carcinoma of the jejunum'; an article by Sircar on 'Intratracheal anaesthesia in surgery'; one by Politzer on 'X-ray diagnosis of mastoiditis'; two articles by Kini, one on 'Myositis ossificans or Traumatic osteoma in the region of the gluteal muscles' and the second on 'Sarcomas of the breast'; and two articles by Bharucha, one on 'A case of cancellous osteoma of the flexor tendon sheath of the left ring finger' and the second on 'A case of spontaneous rupture of a mesenteric cyst'.

\*The Indian Journal of Surgery: A Quarterly Journal. Published by the Association of Surgeons of India. Subscription Rs. 12 per annum. Single copy Rs. 3. Free to members of the Association of Surgeons of India. Annual subscription for membership Rs. 18.

**VENTILATION AND HEATING—LIGHTING AND SEEING. PAMPHLET NO. 1. ISSUED BY THE INDUSTRIAL HEALTH RESEARCH BOARD OF THE MEDICAL RESEARCH COUNCIL.** Published by His Majesty's Stationery Office, London. Pp. 20. Illustrated. Price, 3d.

RESEARCHES in industrial health have shown that unsatisfactory atmospheric conditions and lighting arrangements, besides causing discomfort, lead to reduced production, increased sickness and more accidents. With a view to make the results of research widely known, the Industrial Health Research Board have decided to publish a series of pamphlets in non-technical language, of which this is the first. It is illustrated by photographs, gives an outline of the

known facts on the subject and makes practical suggestions. The importance of making supervision the definite responsibility of one person or group of persons has been stressed, as it has often been observed that the existing systems of lighting, etc., are good but attention to cleaning and maintenance is wanting. There are recommendations for proper lighting installations with a light meter for the satisfactory performance of work. In addition the workers with defective sight and those subjected to close work should be provided with suitable glasses to relieve the strain on their eyes. First-aid treatment should at once be available for any eye accident.

R. N. C.

## Abstracts from Reports

**THE MISSION TO LEPERS: REPORT ON THE 69TH YEAR'S WORK IN INDIA AND BURMA, 1942-43**

This report is always an interesting one and this year the standard is maintained. The report states that in spite of increased expenditure no patient admitted to the homes of the Mission has been turned out for lack of money. Many new applicants however have had to be refused admission. The cost of the work in India for the year has been nearly 8½ lacs.

The report refers to the death of the General Secretary of the Mission, Mr. H. P. Anderson, and to the return from India of Mr. A. D. Miller to take Mr. Anderson's place in London. Mr. and Mrs. Miller's boat was torpedoed and they spent 13 days in an open boat before being picked up.

The Mission has workers in most provinces and many states of India. It maintains 30 homes for lepers in the different provinces and states of India with nearly 6,500 inmates and about 650 healthy children. Aid is also given to 17 other institutions with nearly 2,500 inmates and 140 healthy children. The report gives details of the work done in these homes and gives many personal stories of individual patients. The report is illustrated with photographs and is an attractive publication.

**ANNUAL REPORT OF THE DIRECTOR OF THE PASTEUR INSTITUTE OF SOUTHERN INDIA, COONOR, TOGETHER WITH THE THIRTY-SIXTH ANNUAL REPORT OF THE CENTRAL COMMITTEE OF THE PASTEUR INSTITUTE ASSOCIATION, 1942-43**

THE Pasteur Institute of Southern India, since its inception in 1907, has taken an important part in medical and health work in the Madras Presidency and the Indian States of South India all of which are represented in the Central Committee. Besides anti-rabic work it has, in recent years, undertaken considerable laboratory work and has provided facilities for research.

**Anti-rabic treatment.**—A total of 1,453,615 c.cm. of anti-rabic vaccine was prepared during the year. It is a 5 per cent suspension of sheep-brain (Paris strain of fixed virus) in carbol-saline prepared by Semple's method. Altogether 281 patients received a complete course of treatment at the Institute, while 57 had incomplete courses. There was no death from rabies among the treated patients. The treatment was also given in various subsidiary centres. Out of 10,788 cases, 8,443 had a complete course with 6 deaths, giving a mortality rate of 0.07 per cent. No case of post-treatment paralysis was reported during the year. Anti-rabic vaccine was also supplied for prophylactic treatment of animals. The number of animals treated during the year was 589, of which 495 were dogs.

**Laboratory work.**—Besides routine laboratory examinations for the benefit of hospitals, dispensaries

and practitioners the Institute examined 380 specimens of brains from suspected rabid animals, of which 255 were positive, 13 being unfit for examination.

**Research work.**—An investigation to determine the site of election for Negri bodies in natural and experimental rabies was concluded during the year. In natural rabies, the hippocampus major is in most cases and the cerebellum and mid-brain in some cases were the sites of election, while in experimental rabies the mid-brain, at the level of the oculomotor nucleus, was the commonest site. The Negri bodies were fewer and their size smaller in the brains of vaccinated animals.

The Nutritional Research Laboratory, financed by the Indian Research Fund Association, continued to study the composition of different foods. A simple enzymic method, in which an enzyme prepared from pig's intestinal mucosa is used for extraction of vitamins from test materials, was evolved and used in routine tests for vitamin B<sub>1</sub> and nicotinic acid. In the course of this work it was found that certain raw cereals and cereal products contain a thermolabile factor which destroys vitamin B<sub>1</sub> *in vitro*. Pigeons fed on such cereals however did not develop polyneuritis. Knowledge of the fact that bacteria cannot thrive without vitamins was utilized for delicate quantitative tests for vitamins. Insect larvæ also require vitamin and the larvæ of rice moths are being used for estimation of vitamin B<sub>6</sub>. This will serve as a check on results obtained by the chemical method. The vitamin-A content of 78 samples of animal ghee was determined; the average value of pure cow's ghee obtained from well-fed cows was 34 international units per gramme and that of buffalo's ghee was 10. The vitamin-D content of cow's ghee was found considerably higher than what is reported for butter in England. A study of the nutritive value of dehydrated vegetables was also undertaken; they lose the anti-scorbutic property after a few months. Other work included successful inoculation of rat leprosy on rats receiving a good diet, studies on fluorosis, malnutrition, arbo flavinosis, infantile beriberi, etc.

The Malaria Investigations, financed by the International Health Division of the Rockefeller Foundation, were officially closed down on 31st March, 1942. In its place a new enquiry under the Director, Malaria Institute of India, Delhi, continued to work at the Institute.

## Correspondence

### CONCERNING THE WASSERMANN REACTION

SIR,—In the December 1943 issue of the *Indian Medical Gazette* under the article on 'Concerning the Wassermann Reaction' I fail to see why smallpox vaccination as one of the causes producing false positive reactions has not been mentioned.

Hence will you please publish the following in your valuable monthly:—

False positive syphilitic reactions have been attributed to numerous causes, with smallpox vaccination recently added to the list. Using the Kolmer, Kline, Kinton and Mazzini techniques, Lynen found that pseudo-syphilitic serum reactions developed in 16 per cent of his patients within two weeks after vaccination. The serum usually remained positive for at least two months (*Journal of American Medical Association*, 117, 591, 23rd August, 1941). In order to confirm these data, a group of 202 serologically negative medical students and nurses was vaccinated by favour of Hahnemann Medical College followed by periodic serologic tests with the Kolmer, Kahn and Mazzini techniques. From 14 to 60 days after vaccination 24 of these (11.8 per cent) gave positive pseudo-syphilitic reactions; many of the reactions were of 3 or 4 plus

intensity. All serum became negative by the end of 4 months. (*Journal of American Medical Association*, 123, 97, 1943). The importance of this lies in the fact that a good number of students, suffering from skin diseases of one sort or another, after vaccination (which may be incidental or co-incidental) have been dubbed as having 'bad blood' after the usual serum reactions; thus they have been, by mere blood examination, incriminated. Smallpox vaccination should be kept in mind as one of the commonest causes of producing 'false' positive serum reactions within four months after vaccination.

G. VENKATARAMANIAN, B.A.,  
L.M.S. (Madras),  
Assistant Surgeon and Medical  
Inspector of Schools.

· Mysore City,  
29th January, 1944.

[Note.—With reference to the above letter four points are made by the author of the article (Lieut.-Colonel S. D. S. Greval, I.M.S.):—

(1) The article was virtually completed in 1941 before the author left for active service: it was not revised as it had other ends in view—special features in the technique and special findings in India.

(2) The false positive syphilitic reactions of the *Journal of American Medical Association*, 117, 591, 23rd August, 1941, and 123, 97, 11th September, 1943, appear to be given mostly by the flocculation tests, as opposed to the complement-fixation test: 'I would like to speak of the apparently greater specificity in this study of Kolmer complement-fixation reaction. This observation would further support the view held by many observers that when two or more tests are to be used jointly, one of them should be of a complement-fixation type' (Senear, *Journal of American Medical Association*, 117, 591—Abstract of Discussion).

(3) A post-vaccination period of four months should certainly be remembered when one fails to assign a cause to a doubtful or even a positive Wassermann reaction.

(4) The high percentage of venereal diseases of the lay press, at the present moment, should not be based on flocculation tests done during a period of scare from smallpox.—Editor, *I. M. G.*]

### TREATMENT OF NAGA SORE

SIR.—In their excellent paper on Naga Sore, in the January number of the *Indian Medical Gazette*, Drs. Panja and Ghosh have mentioned my copper sulphate-phenol solution under the heading of treatment.

May I draw attention to a modification of my original solution, recommended by James (1938), which I have found superior. It consists in the substitution of glycerine for water and the formula is as follows:—

R: Copper sulphate	..	..	2½ drachms
Phenol	..	..	1 drachm
Glycerine	..	..	1 oz.

The method of preparing the solution is important. The copper sulphate is well powdered and added to the glycerine; the mixture is then heated and stirred, if necessary it may be brought to the boil, until all the copper sulphate has dissolved. This is best done in a crucible or enamel bowl. When the solution has cooled, the phenol is added.

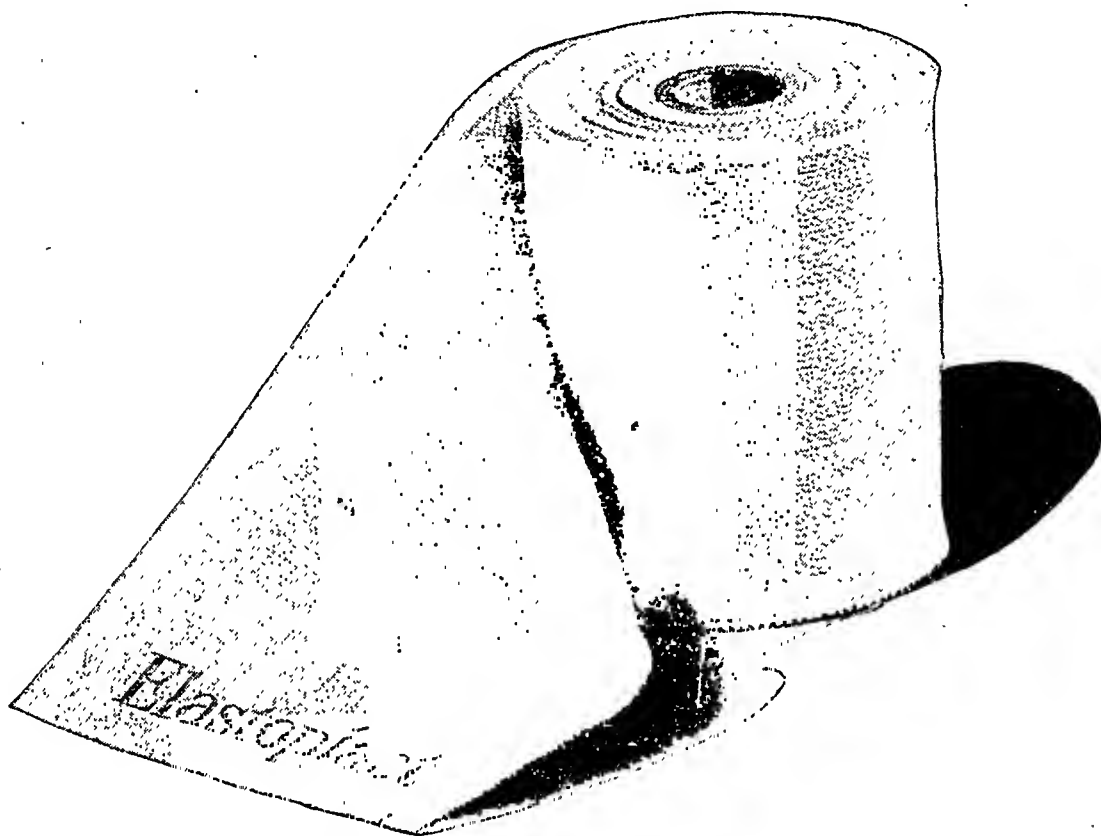
My original solution was made up in water and I recommended that it should be well shaken before use in each case as the phenol was not soluble and rose to the top of the solution; with glycerine substituted, shaking is unnecessary as the phenol is soluble and its full anæsthetic effect obtainable. This is important as these ulcers are extremely painful.

In my practice, where I have seen as many as 2,000 cases a year, the above solution is very popular and

E.B. 9

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almost a specific for removing the slough, which is essential before any further treatment with powders or ointments can be undertaken.

I find that the above solution has been given by Manson-Bahr (1940) with this difference, that all credit has been given to James and none to the discoverer of the original solution! But this is not the fault of James, who in his excellent paper has mentioned that his solution is a modification of my original one.

CHRISTIE MCGUIRE.  
Medical Officer.

NEWLANDS T. E. AND P. O.

DOOARS.

24th February, 1944.

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- JAMES, C. S. (1938) .. *Trans. Roy. Soc. Trop. Med. and Hyg.* **31**, 647.  
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### THE OCCURRENCE OF NAGA SORE IN BENARES

SIR,—I was very much interested to read 'The Report on the Occurrence of Naga Sore in Calcutta' by Drs. Panja and Ghosh. It appears to me that this new disease had spread much beyond Calcutta, for during the last rainy season I saw a number of cases in Benares. Some cases were seen in children of well-to-do people living in hygienic conditions and uncrowded localities. The discharge of more than a half dozen patients was examined by me microscopically, and I found only fusiform bacilli—Gram-positive rod-shaped bacilli tapering at both ends—in abundance. I, therefore, think that fusiform bacilli appear to be responsible for this disease.

B. G. GHANEKAR, B.Sc., M.B., B.S.  
In-charge, Pathological  
Laboratory.

BENARES HINDU UNIVERSITY,  
BENARES.

27th February, 1944.

## Service Notes

#### APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL G. VERGESE, C.I.E., is appointed temporarily as additional Deputy Director-General, Indian Medical Service (Recruitment), with effect from the 10th January, 1944.

Lieutenant-Colonel A. K. Sahibzada, O.B.E., is appointed temporarily as Assistant Director-General, Indian Medical Service (Recruitment), with effect from the 20th January, 1944.

Major (Acting Lieutenant-Colonel) D. K. Lindsay was appointed Chief Medical Officer, Delhi Province, and Civil Surgeon, Delhi, vice Major H. A. Ledgard, granted leave.

#### LAND FORCES—INDIAN MEDICAL SERVICE (Emergency Commission)

##### SECONDED TO INDIAN ARMY MEDICAL CORPS

###### To be Captains

- (Miss) L. C. Peterson. Dated 10th June, 1943.  
I. S. Dalton. Dated 19th March, 1943.  
W. A. Clark. Dated 11th May, 1943.  
J. C. Valentine. Dated 8th August, 1943.  
J. F. R. Bentley. Dated 26th April, 1943.  
H. P. Banerjee. Dated 12th November, 1943.  
Melareode Subramania Ayyar Vaidianathan. Dated 14th December, 1943.  
Archibald Maurice Fratell. Dated 21st December, 1943.  
Taher Tyebally Harianavala. Dated 22nd December, 1943.  
Akhtar Husain. Dated 25th December, 1943.  
Hara Prosad Banerjee. Dated 12th November, 1943.

20th November, 1943

- Pratap Krishna Topa. Hassan Lakshminarayana.  
Pannalal Sharma. Dated 27th November, 1943.

20th December, 1943

- Balai Chand Chatterjee. Kshirode Behari Das.

###### To be Lieutenants

- D. G. R. Fox. Dated 10th June, 1943.  
Dev Nath. Dated 18th December, 1943.  
Ramesh Chandra Sharma. Dated 12th December, 1943.

13th December, 1943

- Conjeevaram Subramaniam Nagarajan and Kiriti Jayavantha Raju.  
Arumungam Venkatachalam. Dated 14th December, 1943.

15th December, 1943

- Dhurjaty Krishna Murthy and George Timothy Joshua.

18th December, 1943

- Salem Narayanawami Venkataraman and Authimoolam Sivabooshanam.  
Mohammad Musharraf Ali. Dated 19th December, 1943.  
Sadiq Noor Sahibzada. Dated 13th November, 1943.

14th November, 1943

- Shori Lal Khosla. Lachman Das Sachdeva.  
Abdul Aziz Awan. Akhunzada Mohammad  
Khaliq Dad Khan, Sher-Yusuf.  
wani. Omer Yacob.  
Mohinder Singh. Gandharv Singh Sarin.  
Baldev Singh Sidhu. Jagjit Singh.  
Khawaja Saeed Hasan. Gurcharan Das Kapur.  
Bashir Ahmad Bhatti. Mohd. Hassan.  
Mohd. Zahir Abid.

- Basharat Ahmad. Dated 14th November, 1943.  
Abdul Ghafoor Sheikh. Dated 18th November, 1943.  
Mohd. Ghias-ud-Din. Dated 19th November, 1943.  
Pathpalli Sarvathammya. Dated 11th December, 1943.  
Sushil Kumar Das Gupta. Dated 20th December, 1943.

#### (WOMEN'S BRANCH)

##### To be Captain

- (Miss) Muriel Marie D'Souza. Dated 13th December, 1943.

##### To be Lieutenants

- (Miss) Hamida Malik. Dated 24th December, 1943.  
(Miss) Tehmina Namdar Irani. Dated 26th November, 1943.  
(Miss) S. L. Bhatia. Dated 18th December, 1943.  
(Miss) P. Vedam. Dated 20th December, 1943.  
(Miss) P. H. Baria. Dated 24th December, 1943.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED FOR SERVICE WITH ROYAL INDIAN NAVY

(Emergency Commission)

To be Captains

Ethelwold Anthony Sequeira. Dated 5th November, 1943.

Do Rosario Fausto Pinto. Dated 6th November, 1943.

To be Lieutenant

Cottur Muthuswamy Chandrasekaran. Dated 19th December, 1943.

PROMOTIONS

Captains to be Majors

S. G. O'Neill. Dated 5th February, 1944.

F. J. Doherty, D.S.O. Dated 5th February, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
(SECONDED TO INDIAN ARMY MEDICAL CORPS)

(Emergency Commissions)

Lieutenants to be Captains

T. R. I. Subramanian. Dated 1st November, 1943.

S. K. Bhattacharya. Dated 2nd November, 1943.

4th November, 1943

A. H. Khokhar. F. M. Graham.

A. J. Ralston.

6th November, 1943

D. R. Aggarwal. F. J. Hopkins Husson.

S. K. Mukherjee. Dated 7th November, 1943.

P. Ray. Dated 10th November, 1943.

B. K. Vaid. Dated 12th November, 1943.

J. R. Samuel. Dated 15th November, 1943.

16th November, 1943

K. Gajjala. M. R. Gopalaratnam.

V. Chittor. O. M. Satyadran.

K. B. R. Rao. Y. P. Naidu.

C. N. N. Nambisan. I. U. Choudhary.

A. K. Choudhary.

17th November, 1943

K. R. Venkatachalapathy. F. A. Khan.

S. P. Gulati. K. S. Kochhar.

K. N. Kotaneth. Dated 19th November, 1943.

N. P. Sen. Dated 20th November, 1943.

27th November, 1943

S. V. S. Krishnan. T. C. Hopkins Husson.

28th November, 1943

L. N. Budhraj. V. L. Srinivasan.

P. R. Naidu.

V. V. M. S. Mudali. Dated 29th November, 1943.

A. K. Sear. Dated 30th November, 1943.

2nd December, 1943

K. K. U. V. Raja. T. Kurunakaran.

A. Ramachandracharya. C. V. David.

R. N. Sil. Dated 4th December, 1943.

S. K. Bhattacharyya. Dated 5th December, 1943.

6th December, 1943

K. P. Mitra. H. W. C. Griffiths.

W. E. Rodgers.

7th December, 1943

B. C. Mitra. J. H. P. Johnson.

8th December, 1943

H. J. Brown. E. J. Frederick.

J. D. V. Fitzpatrick. Dated 12th December, 1943.

C. T. Symonds. Dated 13th December, 1943.

M. P. McMurry. Dated 14th December, 1943.

S. E. Tanner. Dated 15th December, 1943.

W. S. O'Malley. Dated 17th December, 1943.

19th December, 1943

R. M. B. Panhcarwo. G. W. G. Bird.

E. N. Plomer. Dated 23rd December, 1943.

A. C. Bose. Dated 24th December, 1943.

R. H. P. Fitzpatrick. Dated 25th December, 1943.

28th December, 1943

S. Kalyanasundaram. H. P. Granaoliva.

L. N. Gunti. H. D. Grover.

H. R. Jacob. F. J. Satur.

29th December, 1943

B. P. Reddy. P. Krishnaswami.

T. S. Das. M. J. Menon.

K. M. N. P. Mohamed. S. Narayanan.

30th December, 1943

V. S. Raghavachari. S. K. Srinivasan.

(WITHIN INDIAN LIMITS)

M. K. Tukhi. Dated 11th November, 1943.

V. R. Rao. Dated 20th November, 1943.

A. K. Raj. Dated 27th November, 1943.

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## Original Articles

### SEVERE ANÆMIA IN PREGNANCY

By S. N. UPADHYAY, M.B., B.S.

Department of Obstetrics and Gynecology,  
The Prince of Wales' Medical College, Patna

ANÆMIA in pregnancy is an outstanding problem in this part of India. As a direct or predisposing cause of maternal morbidity it stands second to none of the prevailing diseases. While it is quite natural to expect a healthy puerperium in a woman who has enjoyed good health throughout her pregnancy, with a normal hæmopoietic system and a normal amount of circulating blood, in the presence of grave disorders of the blood system, marked vulnerability to the stress of labour and to puerperal infection may be expected. In the most severe cases the mother may be incapable of nurturing the fœtus in the womb.

Osler (1919) described a 'pernicious type' of anæmia complicating pregnancy and puerperium as a rarity, which indeed it appears to be in the temperate zone. In recent years this disease has been studied in great detail in temperate climates as well as in India, and, as a result, interesting observations have been recorded. Conspicuous among the workers are Evans (1929), Wills (1931), Mudaliar and Rao (1932), Mudaliar and Menon (1942), Mitra (1937), Chaudhuri (1939), Napier (1940), Napier and Das Gupta (1942), Davidson *et al.* (1942), Lescher (1942) and Fullerton (1943).

The present stage of enquiry in India may be found fully set out in the *Memorandum on Anæmia in Pregnancy* (Napier and Neal Edwards, 1942), and it will be noted that a study in representative geographical areas is now necessary to collect further information. Meanwhile controversy exists on the question of nomenclature, on the interpretation in particular of sternal puncture findings, and on the exact ætiology of the condition. The usefulness of blood transfusion is undecided; a specific treatment has not yet been determined; the significance, if any, of œdema in the clinical picture has not yet been investigated.

In commencing an investigation on this problem in Bihar, we have been chiefly guided by the said *Memorandum on Anæmia in Pregnancy in India* by Napier and Neal Edwards and *Hæmatological Technique* by Napier and Das Gupta. The work is as yet at an early stage, and one has hesitated to report on the somewhat limited number of cases studied and with ideas on so many aspects of this problem as yet uncertain. However, if reference is made to the excellent informative paper of Mudaliar and Menon (1942) concerning conditions in Madras,

and case notes and reports by Davidson *et al.* (1942) and Fullerton (1943) regarding the course of the disease at Edinburgh and Aberdeen respectively, one may be permitted at this stage to offer some useful comparative figures for the Patna zone, and express the hope that, in due course, from other enquiries similar figures for comparison may appear in the literature.

*The present enquiry.*—In order to appreciate the degree of changes in the pregnant anæmic woman, a very brief account of the normal hæmatology will be given. One of the important steps in proceeding with the study of this disease has been the realization that anæmia as judged by temperate zone and European standards is not an inevitable state in the tropical zone, be it in the pregnant or the non-pregnant individual.

The number of cases examined are 86 apparently normal non-pregnant women of child-bearing age, 51 apparently normal pregnant women and 58 anæmic pregnant women.

The following information has been recorded :—

Age, religion, economic status, diet, gravidity, nature of the previous pregnancy, labour and puerperium (if any).

The findings recorded are :—

(a) Clinical : general condition, œdema, appetite, blood pressure, splenic enlargement, liver, results of detailed examination of each system (e.g. cardiovascular, respiratory, central nervous system, etc.), child, any other special feature.

(b) Hæmatological : hæmoglobin in gramme per c.cm., total erythrocytes, reticulocytes, mean corpuscular volume, mean corpuscular hæmoglobin, mean corpuscular hæmoglobin concentration, mean corpuscular diameter (kalometer), total leucocytes, differential leucocyte count, Arneth count, parasites, any special feature of the smear (e.g. anisocytosis, nucleated red cells, etc.), colour index, sedimentation rate, type of anæmia, sternal smear character.

(c) Biochemical : total nitrogen content of plasma, non-protein nitrogen content of plasma, total plasma protein concentration; van den Bergh reaction—direct : indirect : quantitative estimation of bilirubin per 100 c.cm. plasma.

(d) Wassermann reaction.

(e) Stool and urine.

(f) Effect of treatment on

- I. General condition,
- II. Hæmopoietic system and
- III. Plasma protein concentration.

*The anæmic pregnant women.*—Almost all of these are cases of grave anæmia in pregnancy admitted to the Hospital for Women, The Prince of Wales' Medical College, Patna, by the Patna Maternity Service.

Special attention has been given to the problem of œdema which forms a conspicuous feature of our series, as this is present in all the severe cases encountered in this part of Bihar.

*The blood picture in a normal pregnancy.*—

A comparison of the normal non-pregnant woman with the apparently normal pregnant woman reveals the so-called 'serous plethora' described by Kiswich and attributed by Dieckmann and Wegner (1934) and Bethell (1936) to progressive increase in the blood volume unaccompanied by a correspondingly rapid increase in the cells throughout pregnancy, giving rise to a relative decrease in the number of cells in a fixed volume of blood. This feature was observed in all the normal pregnant women (specially marked during the 26th to 32nd weeks), and has been referred to as 'physiological anaemia' of pregnancy.

An increase in the average size of the red cells with increased haemoglobin concentration has been observed and confirmed by estimations of the corpuscular values. This appears to be an attempt at maintaining the oxygen-carriage mechanism of the available cells in face of the dilution of the blood.

The total plasma protein concentration was found definitely lower than the normal non-pregnant women, though maintained above the lowest normal range.

The van den Bergh reaction gave an impression of an increased bilirubin content of the plasma, not very significant but still worth mentioning.

The blood smear revealed a relative increase of eosinophil cells during pregnancy, together with a minor rise in the reticulocyte count.

The sedimentation rate was found definitely higher in the pregnant women.

Some degree of leucocytosis is invariably present (11,000 per c.mm.) and is perhaps part of a useful and necessary protective mechanism for the prevention of infection. It has been noted (Chatterjee and Mitter, 1941) that haemolytic streptococci of group A have been found in the uterine cervix and vaginal pool of patients whose puerperium has been afebrile and apparently normal. Considering the known presence of highly virulent organisms and the dirty methods of village midwives, it seems certain that the protective mechanism must be specially efficient to prevent an even greater incidence of morbidity and a higher mortality rate.

It is generally accepted that the total blood volume is increased substantially in a normal pregnancy, and the intracellular fluid content of the blood is also increased to some extent in all pregnant women. It is regretted that so far it has not been found practicable, in examining anaemia in pregnancy, to estimate the total blood volume and the total tissue fluid content, and therefore the true state of actual anaemia in any case has not been determined.

The following table shows the mean average of changes in the pregnant women :—

Hæmatological data	Non-pregnant state	Pregnant state
Hæmoglobin (in gm. per 100 c.cm.).	13.519	12.50
Total erythrocytes (in millions per c.mm.).	4.7	4.08
Reticulocytes (per cent of red cells).	0.54	0.9
Mean corpuscular volume (cu. $\mu$ ).	83.9	89.65
Mean corpuscular hæmoglobin (gm. %).	29.38	32.5
Mean corpuscular diameter (micrometer).	7.14 $\mu$	7.3 $\mu$
Sedimentation rate (in mm. for one hour).	16	25
van den Bergh reaction (mg. bilirubin per 100 c.cm. plasma).	0.209	0.30
Total leucocytes (per c.mm.).	6,276	11,258
Eosinophil (per cent)	3	8.7
Plasma protein concentration (gm. per cent).	7.06	6.752

*Anæmic pregnant women.*—Classification : The cases of anaemia studied have been grouped on a practical hæmatological basis, taking into account both the size and the hæmoglobin content of the cells with the possibility of nine different combinations. Of these, macrocytic hyperchromic anaemia is very frequent, and the severe forms belong specially to this group. The following table shows the different types so far encountered :—

	Macrocytic	Normocytic	Microcytic
Hyperchromic	34	5	Nil
Orthochromic	8	5	1
Hypochromic	2	1	2

It has been suggested by some workers that this classification is not satisfactory because of the possibility of a change in the type of blood picture with the progress of a case. Nevertheless, its use has been continued because it is widely used and understood, and the alternative of classification on the basis of sternal marrow studies is not yet beyond the stage of controversy. However, it is recognized that with further experience of interpretation of the results of sternal puncture, an improved and universally accepted classification may emerge.

*Incidence of anaemia in pregnancy.*—It is very difficult to give the figures for exact incidence of anaemia in all pregnant women, as only a small proportion of the population attend the antenatal clinic. Most of the cases received in the hospital are those discovered by the maternity service and sent in for treatment when the disease is advanced. Some degree of anaemia is so common as to be regarded as a usual state in pregnancy, and this is specially the case among the poorer classes who form the bulk of the population.

*Age incidence.*—The majority of cases of anæmia in pregnancy so far encountered are in patients below 25 years of age, which corresponds with the period of maximum fertility, and is much below the age generally met with in pernicious anæmia. The following figures show the distribution of anæmia according to age groups :—

Age groups	Number of anæmic pregnant women
15 to 20 years .. ..	23
21 to 25 years .. ..	16
26 to 30 years .. ..	12
31 to 35 years .. ..	5
36 to 40 years and over ..	2

*Parity.*—Regarding the possible influence of parity, it is noted that more cases were encountered in primigravida, and clinically the degree of anæmia was more severe in the primigravida than in the multigravida. There may be a fallacy arising from the tendency of the primigravida to seek hospital aid more often than the multigravida, but it has long been noted clinically, and the figures tend to confirm this impression, that anæmia in pregnancy is more severe and common in primigravida. In the present series, the distribution of anæmia in relation to gravidity runs as follows :—

Gravida	Number of patients
First .. ..	21
Second .. ..	10
Third .. ..	7
Fourth .. ..	5
Fifth .. ..	6
Sixth .. ..	2
Seventh .. ..	5
Eighth .. ..	1
Ninth and over ..	1

*Seasonal variation.*—The apparently greater incidence of anæmia in pregnancy in certain seasons runs parallel with the increase in the number of confinements, so that a particular season does not seem to play any important part in the causation of anæmia.

*Natural predisposition.*—Enquiry into the past history does not reveal any natural predisposition to anæmia in any of the patients.

*Community : economic level : diet.*—The distribution of anæmia in pregnancy according to the different races is as follows :—

Community	Number of patients
Hindus .. ..	49
Muslims .. ..	8
Others .. ..	1

Compared to the census of 1942, this shows a fairly uniform distribution of anæmia in pregnancy in relation to relative proportion of different races in the population. Among the poorer classes the manner of life of different communities is similar, and no difference in the behaviour of the disease would, therefore, be expected.

In the majority of the cases, the economic status and the nutrition level are inter-related. However, in some of our cases we found the diet deficient, not only in vitamins and minerals but, also in the total calories, in spite of a better economic status. Whenever anæmia developed due to causes other than an acute hæmorrhage, infection or some such other recognizable cause, the diet was invariably lacking either in total values or in balance. Queer combinations in diet sometimes encountered may perhaps make the utilization not only difficult but also trying by its powers of inhibiting the normal gastric functions. So far as this work goes, there is no case of severe anæmia in pregnancy occurring in any woman taking a full ration of milk (one pound daily minimum) together with a mixed vegetable diet. The impression, therefore, is that the choice of diet may be more important than social habit or economic level.

For purposes of classification, diets were divided in the following arbitrary groups, based on a rough idea of the general dietary habits of the population, and the incidence of severe anæmia was found as follows :—

Type of diet	Number of cases of anæmia
1. Sattu, coarsely crushed maize, sweet potatoes, sometimes green leafy vegetables, 'sag'.	32
2. Sattu, coarsely crushed maize, 'khesary' ( <i>Lathyrus sativa</i> ), other types of 'dal', barley and green leafy vegetables every day; occasionally rice.	15
3. Rice, gram, peas, legumes, wheat flour, vegetables, often a little milk, less than $\frac{1}{2}$ lb. daily.	6
4. Rice, wheat flour, dal, vegetables, daily milk, less than 1 lb., sometimes fruits.	5
5. Rice, wheat flour, fruits, daily 1 lb. milk, occasionally butter, fish, meat or eggs.	Nil
6. Rice, dal, wheat flour, vegetables, regular milk more than 1 lb. daily, butter, fish, meat or eggs regularly.	Nil

A great majority of the population live on the first three types of diet. Ordinarily this nutrition level appears to maintain the normal hæmopoiesis, may be at a low normal range. During pregnancy, however, it is essential that a positive nitrogen balance be maintained because of the demand for nitrogen for the growth of the



uterus, the breasts, and the foetus; moreover, losses in the maternal tissues have to be replaced, and a protein reserve for the lactation period has to be established. Naturally the maternal organism suffers, under the physiological stress of pregnancy, on a diet lacking in all types of first-class biologic proteins.

*Clinical picture.*—The one outstanding feature of the pregnant anæmic woman is the calm composure with which she reports herself in the hospital (if not brought in an unconscious state by the maternity service), obviously unperturbed by the generalized œdema, weakness, dyspnœa, marked anorexia and perhaps some other associated gastro-intestinal symptoms.

*Edema.*—In the severe anæmia in pregnancy encountered in Bihar, some œdema is invariably present and seems to be due to the associated hypo-proteinæmia. It appears that with a reduction in the plasma protein concentration by 1 gm. per cent (below the lowest limit of the normal range) œdema may develop. It has been further observed that with the œdema subsiding, the patient is improving in general health and the prospects of recovery are considered to be highly favourable.

*Albuminuria.*—It is very frequently present and is almost always found in severe cases with œdema. Thirty-seven patients of the present series showed albumin in the urine in varying proportions.

*Cardiovascular system.*—With marked œdema, spleen- and liver-enlargement, polypnœa, tachycardia, palpitation, and marked hæmic murmur, a diagnosis of primary heart disease is not uncommonly made. It is only with the disappearance of these signs on recovery that the essential cause can be recognized. In fatal cases of this kind, the lack of post-mortem facilities is particularly unfortunate. Some degree of cardiac dilatation and hæmic murmur is almost always present. The blood pressure is usually sub-normal. The pulse is invariably weak in tone and rapid, but generally regular in rhythm.

*Splenic enlargement.*—This is found in some of the cases without traceable relation to other chronic diseases. In the present series, 14 showed enlargement of the spleen. The worst cases clinically are those with generalized œdema, fever, enlarged spleen, jaundice and terminal diarrhœa. A suspicion still remains that although careful and repeated investigations have given negative results, in these grave cases some other unrecognized disease may be present, such as latent malaria, kala-azar, amœbiasis, ankylostomiasis, or some such other disease process. For the present, the cause of the splenic enlargement appears to be the exhaustion of the marrow, forcing the spleen and the liver to hæmopoietic activity which results in compensatory hyperplasia.

*Gastro-intestinal system.*—Alimentary tract disorders such as marked anorexia are found in

every case. Diarrhœa may be present in some of the cases and, when occurring after delivery, is very exhausting and of grave significance. Anorexia and œdema are found in all cases of severe anæmia complicating pregnancy.

*Blood picture.*—There is a definite uniformity in the hæmatologic characteristics of the severe anæmia in pregnancy; in the majority of instances a macrocytic anæmia is seen with a considerably reduced erythrocyte count, an increased leucocyte count, a reticulocyte count below 1 per cent of the red cells, an increased sedimentation rate, a low plasma protein concentration, and a blood smear conspicuous by the presence of normoblasts, erythroblasts, megaloblasts, macrocytes, dyhæmoglobinized red cells, anisocytosis, poikilocytosis, polychromatophilia and a 'right-shift' in the Arnett count.

*Erythrocytes.*—Twenty-six patients showed a red cell count of 1.0 million or less, sometimes as low as 0.5 million; 16 were between 1.1 and 1.5 millions; 9 were between 1.6 and 2 millions; and the remaining 7 cases had a count below 2.5 millions per c.mm.

*Hæmoglobin.*—The hæmoglobin concentration ranged between 1.6 and 6.5 gm. per 100 c.cm., being less than 4 gm. in 33 of 58 patients.

*The corpuscular values.*—The mean corpuscular volume was found as high as 170 cu.  $\mu$  in the macrocytic group and as low as 43 cu.  $\mu$  in the microcytic group; the mean corpuscular hæmoglobin ranged from 21 to 55  $\gamma\gamma$  in either group. The distribution of cases has been already dealt with elsewhere. The mean corpuscular hæmoglobin concentration was above 32 per cent in the hyperchromic group.

*Leucocytes.*—The total leucocyte count ranged from 3,800 to 18,450 per c.cm., being more than 10,000 per c.cm. in 31 of 58 patients.

*Sedimentation rate.*—It was above 84 mm.; in some it was as high as 180 mm. (one hour).

*Van den Bergh reaction.*—The direct response was present in two, with 2 and 2.5 mg. bilirubin per 100 c.cm. plasma; a biphasic response was given by one with 1.2 mg. bilirubin per 100 c.cm. plasma; an indirect positive response was present in 34, with less than 1 mg. bilirubin per 100 c.cm. plasma; and it was negative in rest of the patients. Nevertheless, if hæmolysis was a permanent feature in the production of the disease, a greatly different van den Bergh qualitative reaction would be expected.

*Plasma protein concentration.*—This was found to vary from 0.7 to 5 gm. per 100 c.cm. plasma, being less than 4 gm. per cent in 47 patients.

*Diagnosis from pernicious anæmia.*—The condition simulates pernicious anæmia in the reduction of erythrocytes, the presence of primitive red cells, and very often in the raised colour index. A routine gastric analysis was not thought necessary in the present work since it has not given any substantial clue to ætiology in the hands of any of the previous workers.

Moreover, some amount of gastric disorder and hypoauidity may be encountered even in a normal pregnancy. We are inclined to believe that, in these cases, hypochlorhydria, if found, has been established as a secondary factor, being the result and not the cause of anæmia (Panton and Tidy, 1911; Hunter, 1923). The spontaneous cure after delivery and the absence of symptoms of subacute combined degeneration, distinguish it from pernicious anæmia, and prove beyond all doubts the temporary nature of the breakdown in the hæmopoietic system.

*Course of pregnancy, labour and puerperium.*—Premature labour is the rule; the worst period is following delivery. The patient may recover if she survives for 72 hours after the labour. Fortunately labour is usually uncomplicated by post-partum hæmorrhage, but the unfortunate patient can ill afford to lose any blood at all. Inertia or exhaustion may supervene: a low forceps delivery may be needed. The patient requires careful restorative treatment with nutritive fluids and sometimes blood or plasma transfusions. We as a rule administer forced sugar water drinks, flavoured with lemon or a little rum; if the patient is, however, unable to swallow, 50 per cent glucose solution is given intravenously.

The fœtus shows no errors of development apart from the effects of prematurity. Puerperal morbidity is very common. This whole subject is so important that it cannot be fully dealt with except at a greater length than is possible here.

*Iron deficiency.*—The question of iron deficiency is interesting. No doubt the administration of iron as a part of treatment is correct, as an actual shortage perhaps exists during the disease process, and new supplies will be required for healthy hæmoglobin synthesis. At the same time, it has been ingeniously observed that an actual shortage of iron in a normal pregnancy does not readily develop because the total amount of iron in circulation is 2.65 gm., with an additional 1.32 gm. in storage. The average amount of iron required for pregnancy including the fœtus and 350 c.cu. of blood loss at the time of delivery is 0.5 gm., or approximately 20 per cent of the circulating blood. Moreover, the amount of iron necessary for pregnancy is equivalent to the amount of iron lost by the menstruation for an equivalent period of time. The available iron in even the poorest diet is more than this daily requirement of 2 mg. per day (Pastore).

*Possible ætiology and therapy.*—Reference has already been made to the occurrence of œdema in all severe cases and to the associated hypo-proteinæmia. It is interesting to note that where the disease is very uncommon, as in Aberdeen (Fullerton, 1943), the cases encountered are very unlikely to have been living under conditions of extreme poverty, grave malnutrition, frequent and early child-bearing in a debilitating hot climate with anæmia-producing

chronic infestations and diseases. Therefore these uncommon but well-studied cases may be taken as 'pure' cases of this disease, in which the whole defect would appear to be within the hæmopoietic system. Moreover, in Fullerton's series, two of the three patients were studied some weeks after the birth of the child. Our experience with large numbers of grave cases during pregnancy in this part of India invariably associated with œdema, has forced on our attention to the study of the production and significance of the œdema. We have seen a case showing at the time of admission a red cell count of less than a million and about 12 per cent hæmoglobin, change from a bed-ridden partially conscious and almost helpless woman to a hopeful patient able to stand and even walk within a few days. She had large doses of Hepatex-T (Evans), and commenced to eat, her œdema disappeared, her strength was returning before any appreciable change in her blood picture occurred. Either she got rid of some toxic influence with the delivery of the fœtus and the placenta, or the ingestion of food gave her strength, or both.

When the patient improves by any method of treatment, we find that the plasma proteins immediately rise or are rising. The reticulocyte response has been poor. We have been interested to observe in Fullerton's article that in his 'pure' cases, he obtained little benefit from the use of crude or pure liver extracts alone, but that his cases did well when he fed them with raw liver—a useful source of protein food, if it can be digested.

Despite the administration of large quantities of liver extracts, both crude and purified, iron and yeast, no response may be obtained. In our cases, whenever Hepatex-T was available it was used on the worst cases, and it appeared to produce benefit when the appetite was stimulated. It has been observed that if the appetite returns and the patient eats well without diarrhœa occurring, recovery may be rapid and ahead of any observable change in the blood picture.

We make the basis of our nutrition of grave cases, the administration of whey (milk protein being most easily utilized), later fortified by egg albumin; whole liver is given as liver juice or salted grilled liver cubes, as digestion permits.

Our patients do well when able to swallow and digest protein; we think that the most severe cases would do well with *concentrated plasma transfusions* if this were available. What then is the possible benefit of the protein food?

(a) It may provide machinery for the recovery and maintenance of water balance in the body, always so greatly changed during pregnancy.

(b) It may compensate for loss of a valuable protein by albuminuria.

(c) It may provide adequate and perhaps specially suitable material for liver metabolism and construction eventually into hæmoglobin.

(d) It may ensure an adequate supply of extra protein for foetal and maternal pregnancy requirements.

In considering these matters, the nature of the so-called toxæmia of pregnancy must constantly be kept in mind, and in the cases examined here it is true to say that if the conspicuous anæmia of the patients was ignored, they could all be conveniently classified as 'pregnancy toxæmia'. The anæmia is, however, too striking a feature to permit this classification, and the blood pressure is usually low, sometimes very low.

Additional methods of treatment are the administration of vitamin B-complex and C supplied as food or medicine, and the use of an acid-arsenic mixture and a mild carminative when solid food is given. Occasionally in 'sluggish' patients, thyroid extract appears to be of benefit and to act as a general stimulant to metabolism.

*Transfusion of blood or its substitutes.*—The usefulness of transfusion of whole blood or other blood substitutes in the grave cases has not been established. The problem is a difficult and involved one. If suitable facilities exist, this form of treatment would be administered by concentrated plasma solution with the addition of whole blood transfusion when the blood hæmoglobin concentration was found to be below 30 per cent of the normal.

At present the hope is that with early recognition and correction of diet and the removal of other disease factors, the development of the anæmia may be held in check, the delivery and the puerperium may be safely accomplished, and that a long rest will be allowed before another pregnancy is permitted to strain the blood-forming mechanism.

*Summary.*—Some 58 cases of severe anæmia in pregnancy received in the Hospital for Women, Patna, have been examined, and the clinical findings compared with the results of investigations of 84 apparently normal non-pregnant women of child-bearing age, and of 51 women in the last four months of an apparently normal pregnancy.

Special note has been made of the occurrence of œdema in all severe cases and the importance of hypo-proteinæmia both as regards the cause of œdema and in relation to prospects of recovery.

#### Acknowledgments

In conclusion, I wish to record my deep sense of gratitude to my professor, Major J. D. Murdoch, I.M.S., for his encouragement and guidance. I am also indebted to Dr. A. N. Sarkar, Dr. (Miss) M. P. John, Dr. K. N. Mitter, and to the staff of the Hospital for Women, for their willing co-operation and suggestions. My thanks are specially due to Professor B. N. Prasad, for his criticisms and guidance, and to Dr. T. N. Seth, for his permission to carry on the nitrogen estimations in his laboratory. My thanks are also due to Principal T. N. Banerjee, and to the superintendent,

(Concluded at foot of next column)

## A CASE OF COOLEY'S ANÆMIA

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THIS rare disease, first described in 1927 and believed to be '... found almost exclusively in children of Mediterranean origin' (Whitby and Britton, 1942), has already had four cases recorded in India. All the four children were Indians; three of them were reported from Bombay (Coelho, 1939; - Patel and Bhende, 1939) and one from Calcutta (Napier, Shorten and Das Gupta, 1939). Napier, Shorten and Das Gupta included a general account of the disease with their case report.

*Case report.*—A. K., age four years. First child. No history of trauma at birth. Was

(Continued from previous column)

Dr. B. P. Varma, for their kind permission to carry on this work; and to the numerous writers of textbooks in obstetrics whose works I have freely consulted.

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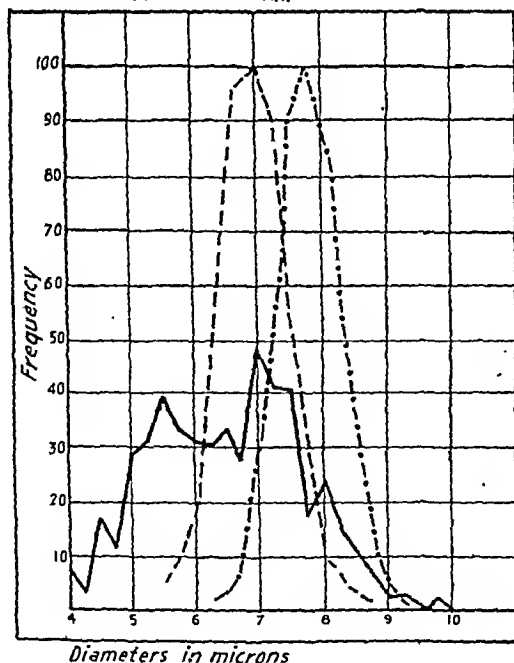
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brought for consultation in summer 1942 on account of pallor, weakness and enlargement of abdomen. Up to ten months of age, the child was reported by the parents to have kept quite fit, but later occasional bouts of diarrhoea and fever occurred. An enlarged spleen had been detected by the parents when the child was one year old; later pallor became more and more marked. About five months before examination, the parents noted a deformity of the shape of the head and a change in facial appearance.

On examination, the child presented a typical 'mongoloid' face. The body was generally wasted but the abdomen was protuberant (see figure 1, plate VII). The weight was 24 pounds. The conjunctivæ bore a subicteric tint. The spleen and liver were enlarged four and three fingers respectively below the costal margin (see figures 2 and 3, plate VII). Hæmic murmurs were audible. No other positive physical findings were detected, no enlargement of lymph nodes, no evidence or history of old fractures. The deformity of the head consisting of protuberance of the frontal bone is well shown in the x-ray photograph (see figure 4, plate VII).

**Blood picture.**—Hæmoglobin—8.7 grammes; red cell count—2.75 millions; mean corpuscular hæmoglobin—31.63  $\gamma\gamma$ ; mean corpuscular hæmoglobin concentration—33.4 per cent; mean corpuscular volume—94.54 c. $\mu$ ; mean corpuscular diameter—6.4905  $\mu$ ; mean corpuscular

Price-Jones' curve of A.I.



Mean cell diameter	..	6.4905 $\mu$ .
Standard deviation	..	1.165 $\mu$ .
Coefficient of variation	..	17.9 per cent.
Mean corpuscular volume	..	94.54 $\mu$ .
Mean corpuscular average thickness.	..	2.8 $\mu$ .
Macrocytosis	..	0.8 per cent.
Microcytosis	..	35.2 per cent.

average thickness—2.8 $\mu$ . Total white cell count 25,250; differential count showed 35 per cent neutrophils, 52 per cent lymphocytes, 7 per cent large mononuclears, and 6 per cent eosinophils; two hundred and four normoblasts and two erythroblasts were seen for a hundred white cells on the average. Marked anisocytosis and poikilocytosis were present; also occasional polychromatophilia; reticulocytes—8 per cent. Van den Bergh—indirect was moderately positive; quantitative estimation of serum bilirubin could not be carried out. Hemolysis started at 0.44 per cent NaCl and was complete at 0.24 per cent NaCl. Wet film showed no abnormality in appearance of red cells. The Price-Jones' curve is reproduced.

*N.B.*—We regret it was not possible to carry out blood examination in a laboratory standardized for hæmatological work. For instance, the Sahli's instrument was not a standardized one. The manufacturer's method of conversion into grammes was used. Similarly the accuracy of volume estimation cannot be relied upon.

No biochemical estimations could be arranged. Bone marrow could not be studied. The radiologist's report runs: 'On examination of the skull one finds practically the whole of the parieto-frontal region to be involved. The intertabular space is widened and is crossed by thin opaque lines which are very closely packed and which give the classical picture of "hair standing on end". The outer table is thinned. The lower part of the diaphyses of the long bones shows coarsening of the trabecular pattern, best seen in the bones about the elbow'.

**Discussion.**—Weighing up all the evidence, there is no doubt in our minds that this is a definite case of what is known as Cooley's anæmia. Age, facial appearance, blood picture (showing a very high normoblastosis, and no evidence of the remote possibilities of acholuric jaundice or sickle-cell anæmia) and radiological appearances are all highly suggestive features. One of us had seen the Calcutta case, and, though the latter was in an older child, the facial resemblance between the two was distinct and a clinical diagnosis of Cooley's anæmia in our case easy. No person in the previous generations of the patient had married a non-Punjabi. The only younger brother of the patient aged two years was investigated and found to be free of any definite signs of the disease.

**Acknowledgments.**—We wish to thank Doctor P. C. Sen Gupta, of the Calcutta School of Tropical Medicine, for drawing the Price-Jones' curve. Thanks are also due to Doctor M. L. Aggarwal, radiologist of Lahore, for reading the skiagrams, and to Doctor Kalyan Singh, of Provincial Laboratory, New Delhi, for letting us carry out investigations in this laboratory.

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# NON-SUPPURATIVE OSTEO-PERIOSTITIS AS A COMPLICATION OF ULCERS AND SKIN INFECTION: A REPORT ON FOURTEEN CASES

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BETWEEN August 1942 and January 1943 a large number of cases of so-called tropical ulcer were admitted into this hospital. A report on them has already been submitted by one of us (Bharucha, 1943). Of these cases, eight developed a peculiar bone complication during the course of treatment, when in all cases the ulcers had reached a stage of healing. Later, six more cases were transferred to this hospital from another hospital with a diagnosis of scurvy with sub-periosteal hæmorrhages. None of these cases had at the time of admission into this hospital any active skin infection, nor had they any clinical signs of scurvy. On questioning them carefully it was definitely established by one of us (E. P. N. M. E.) that all six of them had received minor injuries which had become septic two to three weeks before the onset of their present trouble.

The clinical picture in all these cases was similar. It started with a minor injury which was neglected, e.g. a scratch by a barbed wire, a tick-bite, or a sore or blister from boots. The patient was admitted into a military hospital where the ulcer commenced to heal. It was at this stage that the patient started complaining of pain in one of the long bones, such as the femur or the tibia.

Details of individual cases are given in the following table:—

The following points emerge:—

1. *Age*.—The age of the 14 patients varied from 18 to 25 years.

2. *Occupation*.—Twelve were sepoys, one a labourer and another a water-carrier.

3. *Distribution*.—The long bones alone were affected. In 4 cases more than one bone was affected. Of these 4, one had 4 bones affected (right radius, right ulna, right and left tibiae), one had 3 bones affected (right and left tibiae and right fibula), and the other two had 2 bones affected (in both cases right and left tibiae). The frequency with which the different bones were affected was as follows:—

Right femur	2	Right tibia	5	Right fibula	1
Left femur	2	Left tibia	8		
		Right radius	2		
		Right ulna	1		

4. *Site of ulcers*.—The ulcers which precede the onset of the osteo-periostitis in these cases were distributed as follows:—

Right knee	1	Right leg	4	Right foot and ankle	2
Left knee	2	Left leg	3		

The relation of the position of the ulcers to the bones affected is shown in the table.

5. *Time interval between the onset of the skin lesion and the start of the osteo-periostitis*.—This varied from two to seven weeks.

6. *Trauma*.—In none of the cases was there any history of direct trauma to the bone at the site of the osteo-periostitis.

## Investigations

1. *White cell count*.—This was moderately raised in the majority of cases. It varied from 8,000 to 12,000 per c.mm.

2. *Blood culture*.—This was done in all the cases. In six a growth of *Staphylococcus aureus* was obtained, an incidence of nearly 43 per cent.

TABLE

Number	Age	Time interval since onset of ulcer	Site of ulcer	Distribution of bones affected	Trauma	White cell count	Wassermann reaction	Kahn reaction	Widal reaction	Blood culture
1	19	3 weeks	Right knee	Right radius Right ulna Right and left tibiae	Nil	8,440	— ve	— ve	— ve	<i>S. aureus</i>
2	22	2 weeks	Right foot	Right and left tibiae	Nil	9,000	— ve	— ve	— ve	— ve
3	22	3 weeks	Right leg	Right femur	Nil	10,500	— ve	— ve	— ve	— ve
4	25	2 weeks	Left leg	Left tibia	Nil	6,300	— ve	— ve	— ve	— ve
5	22	7 weeks	Left leg	Left tibia	Nil	5,620	— ve	— ve	— ve	<i>S. aureus</i>
6	20	..	No ulcer	Right radius	Nil	8,400	— ve	— ve	— ve	— ve
7	18	..	No ulcer	Right and left tibiae	Nil	..	— ve	— ve	— ve	— ve
8	25	7 weeks	Right leg	Right and left tibiae Right fibula	Nil	6,450	— ve	— ve	— ve	<i>S. aureus</i>
9	19	3 weeks	Right ankle	Left tibia	Nil	12,190	— ve	— ve	— ve	— ve
10	18	5 weeks	Left leg	Right femur	Nil	9,960	— ve	— ve	— ve	<i>S. aureus</i>
11	18	2 weeks	Left knee	Right tibia	Nil	..	— ve	— ve	— ve	<i>S. aureus</i>
12	24	3 weeks	Left knee	Left femur	Nil	7,800	— ve	— ve	— ve	— ve
13	23	2 weeks	Right leg	Left tibia	Nil	..	— ve	+ ve	..	<i>S. aureus</i> <i>S. albus</i>
14	20	3 weeks	Right leg	Left femur	Nil	12,500	— ve	— ve	..	— ve



Fig. 1.



Fig. 2.



Fig. 3.

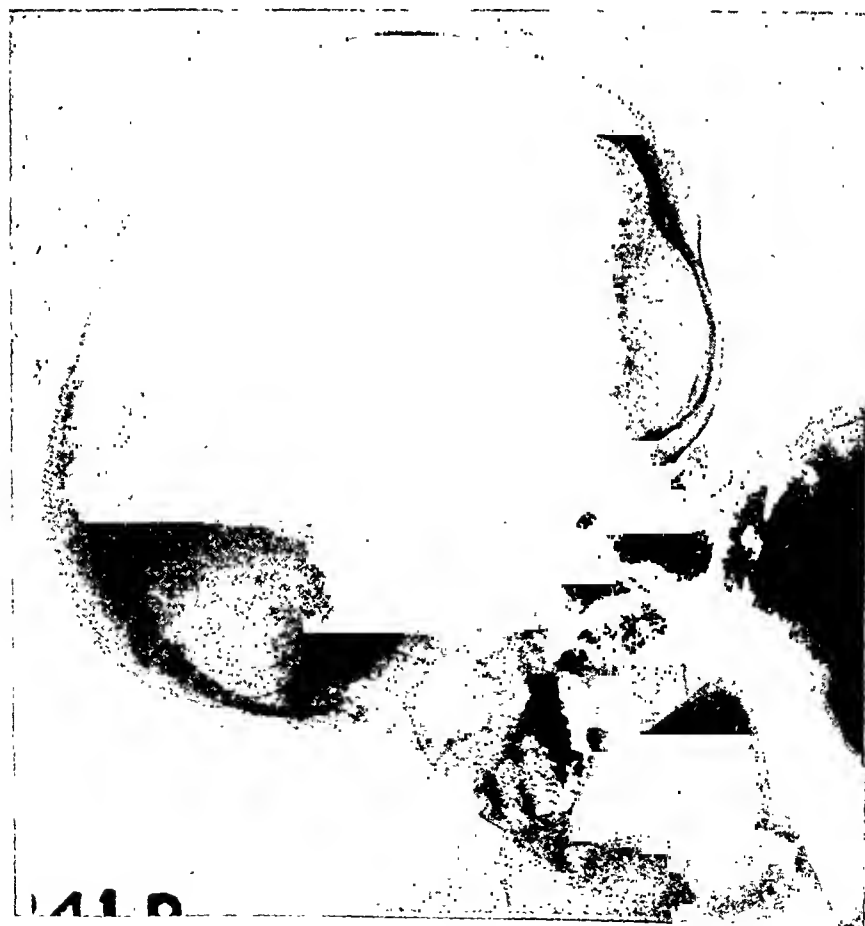


Fig. 4.





Fig. 1.



Fig. 2.

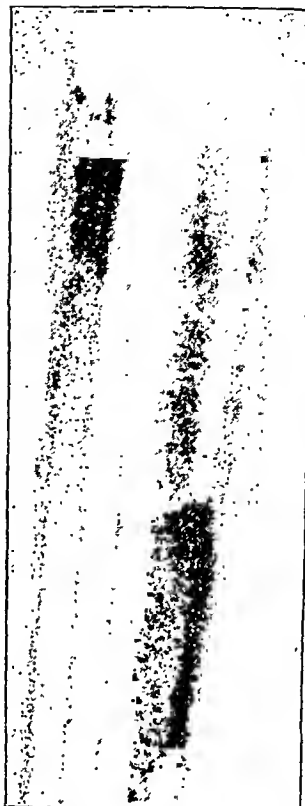


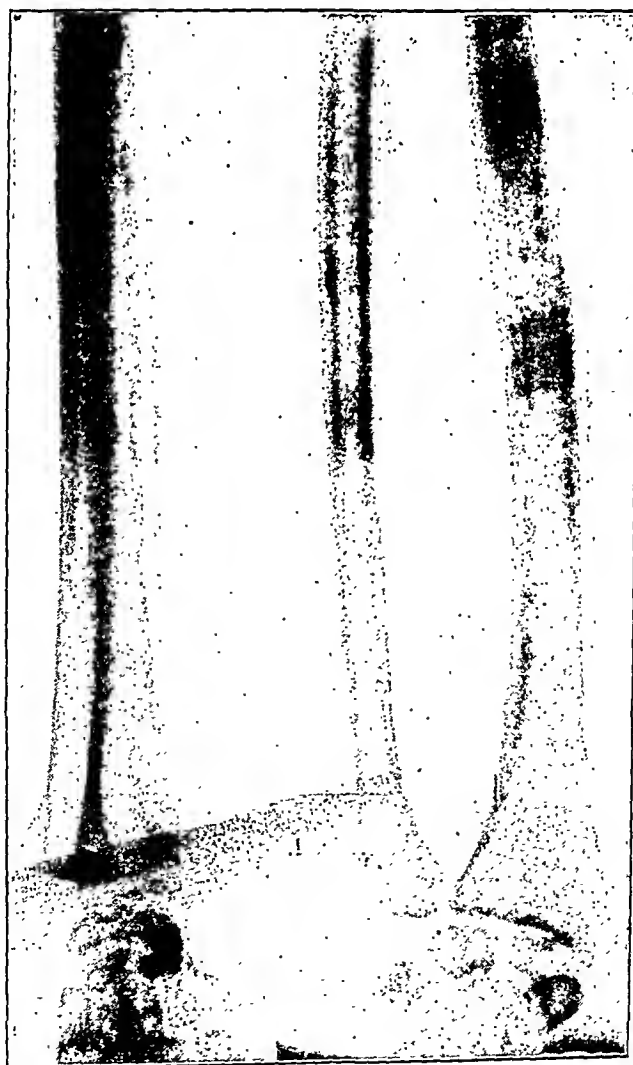
Fig. 3.

Fig. 3.—Showing sub-periosteal new bone formation in the tibia. Medullary space is free. Note that the fibula is also affected.

Fig. 1.—X-ray of the femur showing a comparatively early stage of the disease. The periosteum is raised with new bone formation underneath. The cortex is split into thin flake-like sequestra. The medullary cavity is not involved.

Fig. 2.—Showing extensive involvement of the femur. The cortex is slightly thickened. There are no sequestra and the medullary cavity is not involved.

Fig. 4.—The radius shows extensive osteoporosis with numerous punched-out areas in the cortex. New bone formation is not marked. The medullary space is involved in this case.



3. *Wassermann and Kahn*.—Reactions were negative in all except one, in whom Kahn reaction was 1 plus.

4. *Widal*.—The reaction was similarly negative in all.

5. *X-ray examination*.—(See plate VIII, figures 1, 2, 3 and 4).

We are indebted to Major B. B. Chatterji, I.A.M.C., for the following report on the radiological characteristics :—

(a) Point of origin is at the periphery of long bones. The origin is usually cortical with superficial bone destruction and marked periosteal reaction, which shows a shaggy wavy outline; in a few cases, the density of the thickening suggests periosteal bone formation.

(b) Bone production and destruction are simultaneously noted at the site of mischief, but the destructive process appears to be of the nature of cortical necrosis in small closely separated localized areas which tend to spread superficially along the shaft by marginal coalescence. Sequestra, if present, are superficial, very small and multiple.

(c) No expansion is noted.

(d) The thickened and elevated periosteal lining in some cases is broken through in an irregular manner. The corresponding medullary space in some cases showed inflammatory changes but in a large majority showed no evidence of involvement.

(e) Invasion of the soft tissues was not seen in any of the cases. Actual involvement is first manifested by hazy appearance of the bone outline, and an irregular pitting suggestive of cortical erosion. The concomitant periosteal changes have already been described. When the inflammatory process spreads near the joint spaces, a thin shell of bone remains intact beneath the cartilage.

6. *Bone puncture*.—This was done in one case only. It showed a pure culture of *S. aureus*.

#### *Clinical picture*

This is similar in all cases. About three weeks before the onset of the osteo-periostitis, the patient had a minor injury on some part of the body, which became septic. It is important to note, firstly, that in every case there has been an interval of three to seven weeks between the septic skin lesion and the onset of the bony changes, and, secondly, that in all the cases the skin lesion was in the healing or healed stage at the time the bony changes were noted.

Pain is invariably the first symptom. It begins slowly, is of a continuous nature, and is localized. Later the intensity of pain increases and spreads. It is worse at night and may at times require morphia for relief. After a few days it lessens and again becomes bearable. There occur these periodic exacerbations of pain, sometimes without any apparent reason and sometimes following the taking of unauthorized exercise.

A rise of temperature is present in varying degrees in all cases. The temperature is irregular and varies from 100°F. to 104°F. Increase of pain and rise of temperature go together. Disability of the affected limb varies from total to almost negligible.

The part of the limb affected is always red and warm, but the lymph glands draining the area are not invariably enlarged and painful. The

thickening of the bone can easily be detected in all cases, it being very marked and extensive in some. In a few cases, almost the total length of the tibia or femur was involved.

#### *Pathology*

*Bones involved*.—Only the long bones of the body are affected; those only of the forearm, leg and thigh. The tibia is involved more often than any other bone. It is noteworthy that the fibula which is rarely involved in inflammatory process has been affected once in this series.

The most important point to consider in the pathology of this disease is the channel of infection. It may be either

- (1) direct spread from a neighbouring ulcer, or
- (2) spread via the local lymphatics, or
- (3) by the blood stream.

The first is not very likely, because in none of our cases was there any fixation of the base of the ulcer to the underlying bone, nor was there any close proximity of the ulcer to the affected bone. The second channel is certainly possible, and, as will be seen from the table, such a spread could have occurred in patients nos. 1, 2, 4, 5, 8 and 12. The third mode of spread alone can explain the other cases, namely, nos. 1, 2, 3, 8, 9, 10, 11, 13 and 14. For example, in patient no. 1 the ulcer was on the right knee and in this case the right radius and ulna and left tibia were affected in addition to the right tibia.

The infection seems to have started in all cases under the periosteum and never in the deeper layers of the cortex or marrow cavity, and in all cases it commenced not at the centre of the shaft but towards the ends of the bone.

The local changes were similar in all cases as shown by x-rays. At first there is a lifting of the periosteum, as a result of which the periosteal blood vessels which nourish the superficial layers of the cortical bone are stretched and obliterated; hence the small flake-like sequestra of the superficial cortical bone. At the same time, sub-periosteal new bone formation occurs. All these changes spread both lengthwise and round the circumference of the bone. The whole process is very slow and chronic, and though there do occur exacerbations, frank suppuration has never been found.

The differential diagnosis lies between scurvy, syphilis, typhoid and allied group of organisms and osteo-periostitis of infective origin. Clinically and radiologically none of the lesions in this series resembles those caused by scurvy, syphilis or typhoid.

#### *Treatment*

The treatment of these cases has been very disappointing. In three cases sulphathiazole 20 g. in four days, in three cases sulphapyridine 20 g. in four days and in three cases sulphonamide 20 g. in four days were given without the slightest benefit clinically. All these cases

were strictly confined to bed and the limbs elevated on pillows or Böhler's frames. Rest and elevation of the limb seemed to produce the greatest benefit, but recovery was slow in the extreme, and the slightest attempt at premature resumption of function produced an immediate setback. Operative interference was never considered because of the lack of localization of the lesion. But it has been verbally reported to us that at another hospital one patient was operated upon and an attempt made to remove the sequestra. The result was an onset of septicæmia. Some authorities recommend drilling multiple holes in the periosteum and the cortex, or even chiselling a groove in the periosteum and cortex. It is a method we are very loth to recommend. Heat applied by diathermy is also recommended, but unfortunately we do not possess the necessary apparatus. The treatment indicated in the circumstances obtaining in this command is rest, heat, elevation of the limb, and building up of the body resistance by nutritive diet rich in calcium and vitamin B.

#### Conclusion

Garré describes a condition which he calls non-suppurative osteitis. According to Geschieter and Copeland the main features are :—

- (1) Benign protracted course.
- (2) Age limit under twenty-five years.
- (3) Lesion usually solitary,
- (4) Tibia affected in more than half the cases.
- (5) Acute onset with leucocytosis, rapidly subsiding intensity of disease, but extending over years.
- (6) Pain not severe, worse at night and after exertion.
- (7) X-ray (a) fusiform widening of the shaft by laying down of sub-periosteal and cortical new bone. (b) Cortex thickened and denser than normal. (c) Medullary cavity narrowed and obliterated. (d) No 'onion-peel' formation of periosteum.

These authors also describe an 'ossifying periostitis' as a phase of Garré's non-suppurative osteitis, of syphilis, and of bone and periosteal lesions following typhoid. Their description of this condition differs considerably from that given in this series, in that the lesion in ossifying periostitis is usually single, circumscribed and limited to one surface of the affected bone. The only point of resemblance is that, in 10 per cent of cases, some infection as, for example, boil or carbuncle, is described as present elsewhere in the body.

From a study of this limited series it would appear that the condition described differs in the following respects from that of Garré's classical non-suppurative osteitis :—

- (a) The presence of a demonstrable focus of infection elsewhere in the body in twelve out of fourteen cases.

(Concluded at foot of next column)

## AN UNUSUAL CASE OF CONGENITAL HEART DISEASE WITH 'MIRROR-IMAGE' DEXTROCARDIA (SITUS INVERSUS TOTALIS), FALLOT'S TETRALOGY AND FIRST DEGREE HEART BLOCK

(A CLINICO-ELECTROCARDIOGRAPHIC STUDY)

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(From the Cardiographic Department of the K. E. M. Hospital, Bombay)

CONGENITAL dextrocardia is a term applied to those cases of developmental origin, where the heart assumes a 'right-sided' instead of a 'left-sided' position within the thoracic cage. Of the several varieties of dextrocardia dealt with in present-day treatises on congenital heart disease, the commonest by far is the variety known as 'dextrocardia of mirror-image type' (also referred to as 'dextrocardia with situs inversus of the viscera' or as 'complete heterotaxy'). This form of dextrocardia has been known to clinicians ever since 1643, when Severinus reported its occurrence for the first time. In 1930, Macera and Bordato were able to collect as many as 250 cases of this variety of dextrocardia from the literature.

The 'tetralogy of Fallot' (or 'pulmonary stenosis with inter-ventricular septal defect') is now universally recognized as a fairly common clinical entity of great importance in congenital heart disease. Though first reported in medical literature by Sandifort in 1783, it was not until 1888 that Fallot made the condition well known to the medical profession; three out of every four cases of congenital heart disease with cyanosis observed by Fallot are said to have been of this nature. The 'four' cardinal features of this condition (which constitute the so-called

(Continued from previous column)

- (b) The absence of any encroachment on the medullary cavity in all but one case.

- (c) In four cases out of fourteen the lesions are not single.

- (d) There is no positive history of a previous debilitating disease, and the cases occurred among young and active soldiers.

It is thought possible that we may be dealing with an early stage of Garré's non-suppurative osteitis.

The evidence for the theory that the condition here described is blood borne and metastatic seems fairly strong, and the high proportion of positive blood cultures in which *S. aureus* was found makes it likely that a contamination is not the full explanation. The result of the only bone puncture bears out the hypothesis that the disease is due to a metastatic low grade staphylococcal infection.

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'tetralogy') are: (1) a stenosis, atresia or hypoplasia of the pulmonary artery, (2) an inter-ventricular septal defect, (3) dextro-position of the aorta, and (4) hypertrophy of the right ventricle.

As isolated entities, the above-mentioned developmental defects of the heart (*viz*, dextrocardia and Fallot's tetralogy) are common enough but a coexistence of the two defects in the same individual (as in the present case) is sufficiently unusual to warrant publication.

From the electrocardiographic viewpoint, conduction defects are not very rare in cases of congenital heart disease, the commonest forms of defects being increased auriculo-ventricular conduction time, complete heart-block and bundle-branch block. In the absence of rheumatic infection, the presence of a prolonged P-R interval is very suggestive of an inter-ventricular septal defect (Brown, 1939); its presence in the present case serves to confirm the presence of Fallot's tetralogy, of which condition an inter-ventricular septal defect is an invariable component.

### Case report

R. S., a Christian boy, aged 18, employed in a bakery, was first seen on the 3rd April, 1943, at the K. E. M. Hospital, Bombay. His main complaints were constipation and griping pains in the abdomen. He was born of healthy stock; his parents, brothers and sisters were all alive and in good health; he had always enjoyed perfect health, had never had any pains in his joints or muscles and, in fact, had never been to a doctor. On direct questioning, he admitted having noticed of late some slight shortness of breath on climbing stairs and on walking up-hill. He had never experienced any palpitation or pain in the chest nor had he ever suffered from fainting.

On examination, he was of a thin or hyposthenic build; the fingers and toes showed a moderate degree of clubbing; the nails, lips and mucous membranes of the mouth and tongue displayed a bluish or cyanotic hue. There was no visible pulsation of the arteries or veins of the neck, and the neck-veins were not engorged. Oedema was not observed in any part of the body. The pulse rate was about 70 per minute, the rhythm being quite regular. The blood pressure was recorded as 98 mm. systolic and 66 mm. diastolic.

The apex beat was clearly visualized in the 5th right space,  $3\frac{1}{2}$  inches from the mid-line and just internal to the nipple line. On palpation, the position of the apex was confirmed and a systolic thrill was detected over the upper three interspaces on the right side, the site of maximum thrill being in the 2nd right space, 1 to 2 inches from the lateral sternal margin. Percussion revealed a normal-sized heart situated on the right side. On auscultation, a loud and harsh systolic murmur was heard all over the precordium, the site of maximum intensity of the murmur coinciding exactly with that of the thrill; the murmur was well conducted into the vessels of the neck and could be heard at the back, between the vertebral borders of the scapulae. The first sound of the heart was entirely replaced by the murmur; the second sound, though audible in the basal areas, was markedly reduced in intensity. The liver and spleen were neither enlarged nor tender.

Radiographic examination (see figure 2, plate IX) showed a 'mirror-image' type of dextrocardia, the heart being normal in size but with the apical region on the right side. The configuration of the heart was of the 'cœur en sabot' type with a blunt, rounded and 'upturned' or 'uplifted' apex (probably from right-

ventricular hypertrophy). The stomach bubble was visualized on the right side and the caecum on the left.

An electrocardiogram, taken on 3rd April, 1943, displayed the following abnormal features: (1) Inversion of the P and T deflections of lead I. (2) Inversion of and increase in amplitude of the P waves in leads II and III. (3) Increase in the duration of the P-R interval (0.32 sec.). (4) Upwardly directed ventricular complexes (QRS) in lead I. (5) Very tall, diphasic QRS complexes in the standard leads (figure 1, plate IX).

### Discussion

The existence of situs inversus totalis, in the present case, was proved quite conclusively by (1) the demonstration of the apex beat on the right side, in the 5th space,  $3\frac{1}{2}$  inches from the mid-line, (2) radiological examination of the chest, which not only proved the right-sidedness of the heart but also showed the arch of the aorta on the right side, the stomach bubble on the right side and the shadow of the caecum on the left and (3) electrocardiographic evidence in the form of 'inversion of all complexes or deflections in lead I' and 'an interchange of leads II and III'. The QRS complex of lead I is nearly always directed downwards, in cases of congenital dextrocardia, though exceptions have been reported by Abbott and Moffatt (1929) and by Banerjee (1935). In the case reported here, the QRS complexes were directed upwards in lead I, probably because of the associated tetralogy of Fallot which is known to cause the most extreme degrees of right axis deviation.

The coexistence of Fallot's tetralogy, in the present instance, is proved by (1) the presence of cyanosis and clubbing, (2) the demonstration of a systolic thrill in the 2nd right space or pulmonary area (the change of side being attributable to the dextro-position of the heart), (3) the demonstration of a systolic murmur all over the precordium but maximal in the area corresponding to the pulmonary area (2nd right space, 1 to 2 inches from the lateral sternal margin), (4) conduction of the murmur along the vessels of the neck, a feature of importance, according to Laubry and Pezzi (1921), in the diagnosis of Fallot's tetralogy, (5) the marked reduction in intensity of the second heart sound at the base, (6) the radiological demonstration of right ventricular hypertrophy with a cœur en sabot type of cardiac configuration and a blunt and rounded apex lifted well above the level of the diaphragm. Though the majority of observers (*e.g.* Assmann, 1928; Bedford, 1929; Blackford, 1930) have described, in cases of Fallot's tetralogy, a prominent concavity along the left cardiac border in the region of the pulmonary arc, such a concavity has been reported as missing or inconspicuous (as it was in the present instance) on several occasions (Usunoto, 1925; Bedford, 1929), and (7) electrocardiographic evidence in the form of right axis deviation, high voltage and diphasic nature of the QRS complexes, exaggerated or large P waves in all the leads and increase in duration of the P-R interval. Abnormally tall ventricular complexes

are regarded, nowadays, by the majority of cardiologists as a little suggestive of congenital heart disease; Roesler and Kiss (1931) have drawn attention to the frequency with which diphasic QRS complexes occur in cases of congenital heart disease. According to Brown, exaggerated or large P waves are observed in about 20 per cent of cases of congenital heart disease, and occur with special frequency in the cyanotic group of cases, in which auricular hypertrophy is common. Increase in the duration of P-R prolongation of the auriculo-ventricular conduction time is said to weigh in favour of a diagnosis of inter-ventricular septal defect provided that the possibility of active rheumatism is properly ruled out (Brown, 1939). Inversion of the P waves in leads II and III (as in this case) has been recorded previously, in cases of congenital heart disease, on rare occasions.

### Summary

The case, reported here, of multiple developmental defects of the heart, is unique in that it presents a most unusual combination or association of heart lesions: (1) a complete transposition of all the viscera, with the 'mirror-image' type of dextrocardia, (2) Fallot's tetralogy (which includes besides stenosis or atresia of the pulmonary artery, an inter-ventricular septal defect, dextro-position of the aorta and hypertrophy of the right ventricle) and (3) a partial or first degree heart block, with an increased P-R duration of 0.32 second. Other features of interest in this case are: (1) the inversion of P waves in all the limb leads of the electrocardiogram, (2) the lack of concavity of the cardiac silhouette in the region of the pulmonary arc, and (3) the extensive audibility of the systolic murmur, which could be distinctly heard all over the chest.

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## EVALUATION OF GRUSKIN'S INTRA-DERMAL TEST FOR PREGNANCY

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THE need for a satisfactory test for pregnancy has long been felt, and numerous tests have been evolved for this purpose. A few of these may be mentioned.

The Aschheim-Zondek (1928) test or its modifications depend on the demonstration of the anterior-pituitary-like hormone in the urine of pregnant women. Though this is widely accepted as the most accurate and certain test, it has several disadvantages, in that it is expensive, complicated, and entails the maintenance and use of test animals. (In the Aschheim-Zondek test, white mice are used, and in the Friedman (1929) modification, rabbits are used as test animals.) In the Bitterling test, (Gottlieb, 1936) standard Japanese Bitterling fish are used. The fish are placed in a bowl containing a known quantity of water and pregnant urine, and observations are made at 24-hour intervals. In positive cases there is enlargement and lengthening of the ovipositor. This test is again complicated and entails the maintenance of the standard type of fish.

The detection of histidine (Vanrell and Miserachs, 1935) in the urine of pregnant women as a possible method of diagnosis has been commented on by several workers.

The need for a simple, inexpensive test is apparent. Of the intradermal tests, the test of Benjamin Gruskin (1936), subsequently confirmed by E. Schwartz (1936) and G. Pangalos (1939), deserves attention. Gruskin based his test on previous work done by himself (1929, 1932, 1933) concerning the nature of homologous proteins producing an allergic reaction with the formation of weals with 'pseudopodia' when injected intradermally in cases of malignancy. He applied the same principle to the diagnosis of pregnancy, utilizing placental tissue as antigen, which when injected intradermally produced weals with pseudopod formation at the site of injection in pregnant women. Pseudopods did not appear when there was no pregnancy. It has been proved that this reaction is due entirely to the allergic response on the part of the individual to an homologous protein. The test is positive during menstruation on account of the decidual involvement of that process which will respond to the homologous protein of the placental extract. Gruskin also found that this test, like the Aschheim-Zondek test, gave positive results in teratomas on account of the foetal character of this type of tumour.

The intradermal test discussed in this paper is a continuation of the experimental work done



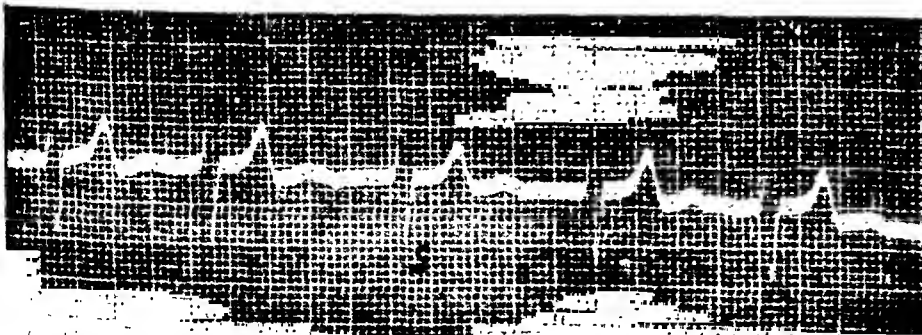
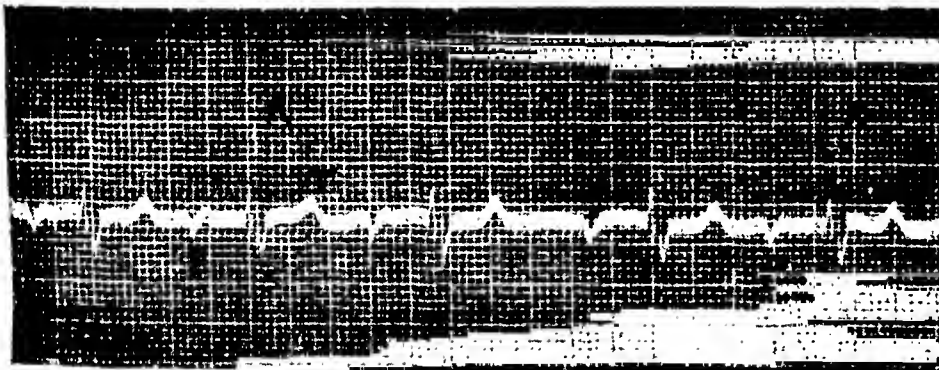
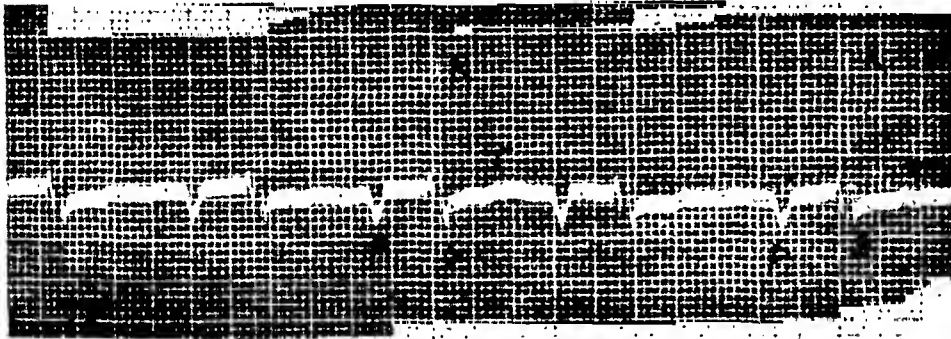
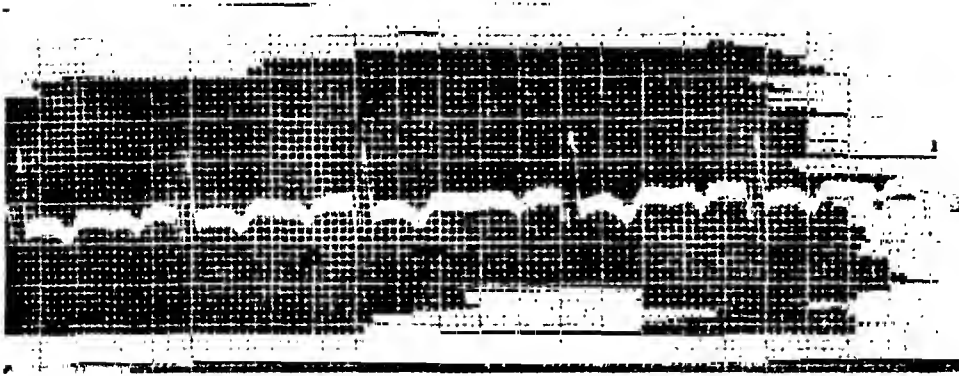


Fig. 1.

Electrocardiogram (3-4-43) shows inversion of P and T waves in Lead I, increased duration of P-R and tall, diphasic QRS complexes in the limb leads.

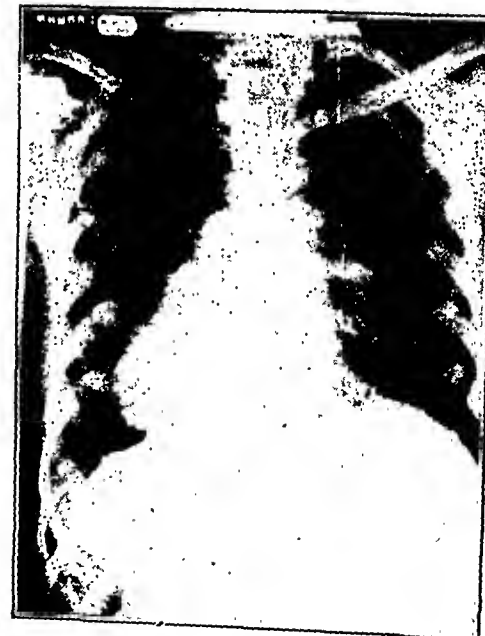
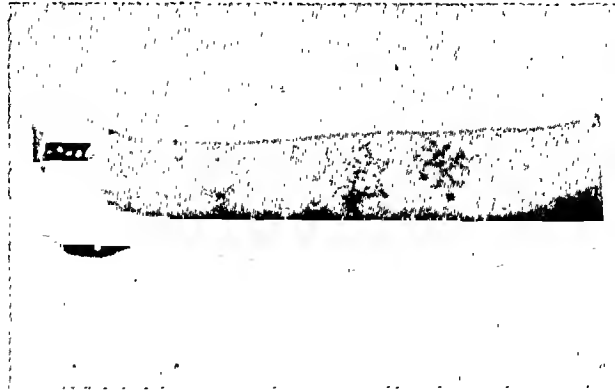


Fig. 2.

Dextrocardia cœur en sabot.



PLATE X  
EVALUATION OF GRUSKIN'S INTRADERMAL TEST FOR PREGNANCY :  
V. R. NAIDU & C. D'SOUZA. PAGE 204



Photograph of a weal produced by intradermal injection of antigen. Note the wavy outline owing to the formation of 'pseudopods'.

TRAUMATIC CEREBRAL HERNIA : HALDER. M.H.P. (PAGE 224)



by Gruskin, and the placental antigen used in our cases was prepared by us in the Pathology Laboratory of the Medical College, Mysore, according to the method outlined by Gruskin.

#### *Technique of test*

The skin over the volar aspect of the forearm is cleaned with alcohol and dried lightly with sterile gauze.

One-tenth of a cubic centimetre of antigen is injected intradermally with a tuberculin syringe using a fine needle (27 gauge).

In every case as a control we injected a similar dose of physiologic saline solution. The control injection may be done on the same forearm a little distance away from the site of injection of the antigen, or on the opposite forearm. A different syringe is used.

A weal is formed at the site of injection of the antigen. It must be perfectly round and have the appearance of 'orange peel' or 'pig skin' due to the hair follicles. This characteristic appearance of the weal assures one that the antigen has been injected intradermally. In positive cases, a small areola of inflammation and pseudopods appears within 10 minutes (see photograph, plate X).

In negative cases no such reaction takes place, and the weal remains unaltered.

The saline control test must always be negative and show no inflammation or pseudopod formation. The injection should not be forced. If this precaution is not taken, the value of the test is negated by the appearance of false pseudopods.

#### *Fallacies*

(1) As already stated the test is positive during menstruation.

(2) False positive results may occur if the injection is forced.

(3) If the saline control shows pseudopod formation, it can be inferred that the patient's skin is hypersensitive and is not suitable for the test.

#### *Preparation of antigen*

Fresh placentas are necessary for preparation of the antigen. They must be obtained as soon as possible after delivery, thereby avoiding any change which might take place by disintegration of the proteins.

(1) Placentas are carefully washed, and freed as thoroughly as possible from traces of blood and blood clots.

(2) They are cut up into small bits, minced in a fine mincing machine, and finally ground into pulp in a mortar.

(3) The pulp is placed for 24 hours in three times its volume of acetone.

(4) The acetone is poured off and the tissue allowed to dry. It must be rendered free from traces of acetone, by evaporation.

(5) It is then extracted with deci-normal sodium hydroxide solution for 24 hours. In this step the tissue will have completely disintegrated

and gone into solution, which will be highly alkaline in reaction.

(6) It is now neutralized with a buffer solution of the following composition: 0.05 normal hydrochloric acid + 2.27 gm. potassium dihydrogen phosphate per litre of the solution.

The antigen must be brought to a pH of 6.9. This is done by taking 10 c.cm. of the solution and adding the buffer drop by drop till the colour matches with that of a standard coloured solution of pH 6.9 in a colorimeter. The total quantity of buffer now needed is thus easily estimated.

(7) A preservative must be added to the antigen. This is made by mixing two parts of glycerine with one part of merthiolate. Six drops of this mixture are added for every 10 c.cm. of the antigen.

(8) The antigen is placed in sterile pyrex flasks (ordinary glass gives up alkalies and changes the pH), the mouths being plugged with sterile cotton-wool.

#### *Results*

The following were the results of the test done on 126 cases, the saline control tests being negative in every case.

Type of cases	Number of cases	Results
1. Male students of the III and IV Year M.B., B.S., and male attenders in Pathology Laboratory ..	26	Negative.
2. Amenorrhœa due to causes other than pregnancy :—		
(i) Amenorrhœa, 1 year's duration ..	1	Negative.
(ii) Amenorrhœa, 2 months' duration ..	1	Negative.
(iii) Amenorrhœa, 1½ months' duration ..	1	Negative.
3. Menstruating women ..	3	Positive.
4. Missed abortion, term 3½ months ..	1	Positive.
Missed abortion, term 4 months ..	1	Positive.
5. Pelvic cellulitis (case delivered 3 months prior to test) ..	1	Negative.
6. Ectopic pregnancy ..	1	Positive.
7. Pregnant women :—		
(i) Term 2 months ..	6	Positive.
(ii) Term 2½ months ..	2	Positive.
(iii) Term 3 months ..	8	Positive.
(iv) Term 3½ months ..	1	Positive.
(v) Term 4 months ..	5	Positive.
(vi) Term 4½ months ..	3	Positive.
(vii) Term 5 months ..	7	Positive.
(viii) Term 6 months ..	11	Positive.
(ix) Term 6½ months ..	3	Positive.
(x) Term 7 months ..	4	Positive.
(xi) Term 7½ months ..	4	Positive.
(xii) Term 8 months ..	12	Positive.
(xiii) Term 8½ months ..	4	Positive.
(xiv) Term 9 months ..	18	Positive.
(xv) Term 9½ months ..	2	Positive.
TOTAL ..	90	All positive.

In this series five had a Friedman's control test along with the intradermal test and the results agreed. In our experience, correct interpretation of the results depended upon a rigid observance of the technique of intradermal injection, the use of a saline control for every case, and the frequent checking and maintenance of the pH of the antigen at 6.9.

#### Discussion

The intradermal test has several noteworthy features which make worth while its practical application for the diagnosis of pregnancy. These are the inexpensiveness and simplicity of the test, the rapidity with which diagnosis can be made, and lastly the high degree of accuracy of results.

(1) When compared with other standard tests such as the Aschheim-Zondek and Friedman and Bitterling tests, the intradermal test is relatively inexpensive. It does not entail the maintenance of test animals such as guinea-pigs, rabbits or fish. The placental antigen can be easily prepared and stored according to the method outlined by Gruskin. It is one of the cheapest tests. The technique of the test is extremely simple, and one need not go through the ritual of injecting animals and sacrificing them a few days later as in the other tests.

(2) Diagnosis can be made within 10 minutes of the intradermal injection. This rapidity of diagnosis is of the greatest value in conditions such as ectopic pregnancy, especially when a differentiation has to be made between emergency conditions such as ruptured tubal pregnancy and any other acute abdominal catastrophe.

(3) Regarding the accuracy of the test, we have had correct results in all our cases; but we wish to emphasize that the fallacies should be borne in mind. Erroneous results are avoided by adhering to the proper technique.

#### Conclusion

(i) A series of 126 cases was tested with Gruskin's intradermal test of which 26 were controls.

(ii) The tests were done according to the technique described, and were found to be as sensitive as any of the Aschheim-Zondek modifications.

(iii) The utility of test is in (a) its simplicity of performance, (b) the rapidity of diagnosis, and (c) the high percentage of accuracy.

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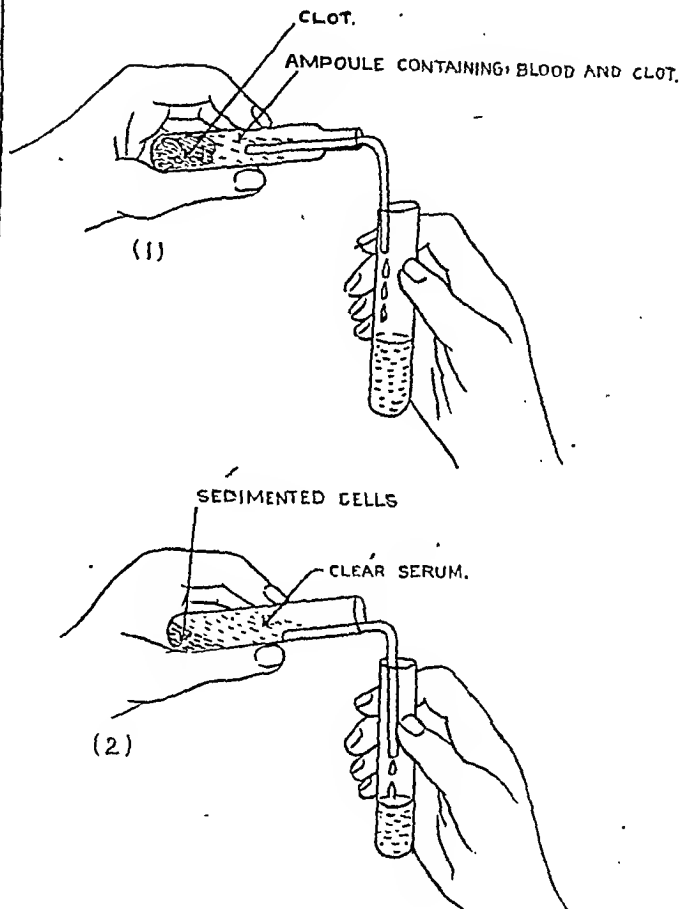
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### A SIMPLE ARRANGEMENT FOR TRANSFERRING BLOOD AND SERUM FROM CAPSULES INTO TUBES FOR SEROLOGICAL TESTS WITHOUT THE USE OF PIPETTES

By N. SESHADRINATHAN, M.B., B.S., D.T.M.  
 (From the King Institute of Preventive Medicine, Guindy, Madras)

Blood samples are usually sent to the laboratory in glass ampoules. On arrival at the laboratory, after being recorded and numbered, the serum mixed with the blood cells is transferred from each ampoule to testing tubes usually by pipetting off with Wright's pipettes. When a



- (1) A simple method of transferring blood from blood capsules arriving at the laboratory for serological tests.  
 (2) Clear serum after centrifugalization of the blood serum mixture.

large number of samples have to be handled, this process is tiresome and takes a lot of time. A large number of pipettes have to be used. Washing is usually a messy process, and very

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## SOME COMMON MISCONCEPTIONS OF MALARIA

By JOHN LOWE, M.D.

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TIMES of stress tend to produce false prophets teaching doubtful doctrine. With malaria widespread and severe, with quinine and the synthetic antimalarials in short supply, some doctors and even some laymen have put themselves forward as malaria specialists, and have made very questionable statements regarding malaria in medical discussions, in medical journals, or in the lay press in India, where even medical men have aired ideas which are quite unsupported by reliable evidence. Some of these ideas are old; some are new; some of them are partly or even completely wrong; unfortunately many obtain considerable publicity and acceptance.

*(Continued from previous page)*

often it is difficult to avoid carrying some serum from one sample along with the washing water into the next sample. Washing also involves much time and labour. If washing has to be avoided, individual pipettes will have to be used for each sample. When about three hundred blood samples a day have to be dealt with, not less than 600 pipettes will be needed every day.

A very simple device avoids all this difficulty and ensures sterility as far as the process of separation is concerned and saves considerable time and labour. In using the device, very much less skill and training is required than in the use of Wright's pipettes.

Small L-shaped glass rods (the broken pieces from Wright's pipettes sealed at both ends may be used for the purpose), of diameter about 1.5 mm. and about 4 cm. for each arm, are used to transfer the serum cell mixture. These are sterilized in packets ready for use. The packets are opened and one by one the rods are picked up with forceps previously sterilized in the flame and one end is introduced into the open end of the capsule containing the blood sample. The illustration explains the process of transfer of the blood serum. The capsule should be opened by breaking the stem as low as possible to enable the blood to flow freely by capillary action along the side of the L rod. When the serum cell mixture has been centrifuged, the transfer of the clear serum can be effected in the same way. A little care, however, is necessary to see that the tube containing the cells and serum is tilted back when all the transferable amount of clear serum has been transferred, to prevent the cells falling into the tube receiving the serum.

This method has been successfully used in the serological section of the King Institute, for the last few years.

This article is not intended for the genuine specialists in malaria, for they will have already realized the importance of most things said

here. It is intended primarily for those who have relatively little experience of malaria, but who in these days of widespread and severe malaria find themselves faced with the problem of diagnosis and treatment of malaria in this country.

It however does attempt to outline and emphasize certain facts about malaria which, while they are stated in modern textbooks on tropical diseases, are often insufficiently emphasized; an understanding of these facts is considered essential to the correct diagnosis and to the wise handling and treatment of cases of malaria in this country at the present time.

In our present discussion we will confine ourselves to malaria due to *P. vivax* and *P. falciparum*. The other plasmodia, *P. malariae* and *P. ovale*, are rare and we need not consider them here.

*The wide variations in the severity of malaria.*—Many doctors do not realize how vastly some cases of malaria may differ from others, how clinical manifestations of malaria may be of almost infinite variety, how malarial infection may be subclinical or rapidly fatal, and how methods permissible in handling one type of case may be fatal when applied to another type of case. Examples of this will be quoted later. It is very foolish to make general statements about malaria except on the basis of a wide experience of malaria of all types.

The two main factors influencing the severity of attacks of malaria are: (1) the species and the strain (or strains, for there may be more than one) of the parasite, and (2) the degree of immunity, natural or acquired, of the individual affected.

*P. vivax* infection can cause an attack of high fever which has very marked tendency to recurrence, and can produce much disability, weakness and anaemia, but it is believed that it practically never gives rise to cerebral malaria, 'algid' malaria and other dangerous forms of malaria, and practically never itself causes death. Malaria due to *P. vivax* infection is fairly constant in its clinical manifestations, and diagnosis presents few difficulties.

*P. falciparum* infection on the other hand, particularly in its severe forms which are now common, is an extremely treacherous and dangerous disease which, if there is any delay in diagnosis or any unwisdom in handling or treatment, may cause death. One can take no liberties with this infection. Moreover, the forms of malaria caused by this parasite are so widely variable that diagnosis often presents considerable difficulty. In fact, in areas where malignant malaria is common (and such areas are now numerous in India), it is good practice in the malaria season to regard almost any acute illness as possibly malarial until proved otherwise.

Another point which is not sufficiently emphasized is the difference between malaria in relatively immune persons and malaria in non-

*immune persons.* The fact will be fully realized from even a limited experience of malaria as seen in the large number of people whom the war has brought straight from non-malarious countries or regions into a highly malarious region. In such persons, the malaria seen is often of a very severe nature, whereas in persons who have lived for some time in a malarious country, the forms of malaria tend to be milder because of a certain degree of immunity that these persons have acquired. Even here it should be remembered that this immunity is an immunity to the strain of parasite with which they happen to have been infected. If they move to another area where different strains of parasites are found, or if a new strain of parasite is brought into the area in which they are living, they tend to get malaria more closely resembling that seen in non-immunes. Both these factors are now operating. Bodies of people are moving from one area to another; new strains of parasites are being carried from one part to another; these facts are contributing to the recent high incidence of malaria in its relatively severe clinical forms.

*The periodicity of malarial fever.*—It was long ago shown in experimental malaria, and later in naturally acquired malaria, that *fresh* infections of malaria are rarely characterized by the occurrence of fever with a 48-hour periodicity. Actually in two-thirds of cases of freshly acquired malaria, the fever to begin with is quotidian or irregular. In *P. vivax* infection it is usually intermittent, but in *P. falciparum* infection it is often remittent and often, to begin with, continuous. It is only after fever has lasted several days, and also in relapses, that the 48-hour periodicity appears. It will therefore be seen that if too much importance is attached to a 48-hour periodicity of the fever and to the intermittent nature of the fever, the diagnosis of malaria will be missed in many cases, including many dangerous cases of *P. falciparum* infection in which a few hours' delay in diagnosis may prove fatal.

Further, too much attention should not be paid to the time of day at which an attack of fever occurs. Malarial rigors may occur at any time of the day or night, and while it is true that they tend to occur earlier in the day than rigors due to other causes, the statement often made that they usually occur before midday is probably untrue in India at any rate, where the early afternoon is the commonest time.

*The importance of examination of blood films.*—These facts all bring out the importance where possible of examination of the blood in the diagnosis of malaria. It is not meant to imply that skilful clinical examination cannot make diagnosis fairly accurate, but it is obvious that if possible it should be supplemented with blood examination. One is sometimes met with the objection, even from doctors with a microscope and stains at their disposal, that they have not time to examine blood films. This objection was never a very strong one, for in

the writer's experience the time spent is most amply repaid by the time saved by the increased accuracy and speed of the diagnosis; but now with the introduction of methods of making and examining blood films whereby several thick blood films can be made, dried, stained, and examined within a few minutes, the objection is very weak indeed.\*

Another point which deserves comment is the misleading idea that untreated cases of malaria in which parasites cannot be demonstrated in the blood are quite common. In a fairly wide experience, the present writer has never seen such a case, if the thick blood film has been properly made, stained and examined, the blood examination being repeated if necessary. He does not say that such cases do not occur; he merely says that he has not seen one and believes them to be very rare. It is therefore believed that the administration of quinine to patients with an undiagnosed fever, who show no parasites in the peripheral blood, is a waste of time and a waste of quinine. In such cases, quinine should be withheld, and further investigations, including blood examinations, made. It is deplorable in these days of quinine shortage to see patients with typhoid fever, kala-azar, dengue, pulmonary tuberculosis, and in fact almost any febrile disease, given quinine for several days, either because a blood examination is not done, or else because a negative report is not regarded as excluding malaria. It is however true that in some cases of heavy infection with *P. falciparum*, the parasites in the peripheral blood may become very few in the period immediately before the rigor, because most of them are then maturing in the internal organs; but, even in such cases, parasites can usually be detected without much trouble by thick film examinations.

Then there is the commonly held opinion that, once a patient has had a few grains of quinine, even if he has malaria, the peripheral blood will often show no parasites. Recently in a medical journal the writer read a statement that after 5 grains of quinine in a case of malaria the blood often became negative. This is nonsense. Again and again experiments have shown that even with full doses of quinine, the parasites do not usually disappear from the blood for 3 days. If a patient comes with a history of recent fever and of having taken a few grains of quinine, a negative film will nearly always rule out malaria.

The adoption by some hospitals of the policy of giving quinine only if parasites have been seen in blood films has not only saved much quinine (75 per cent in one hospital) but also made possible more thorough treatment of genuine malaria.

Recently several articles have appeared in medical journals suggesting that in some cases

\* See this journal (1) vol. 77, December 1942, p. 725; (2) vol. 79, February 1944, p. 73 and (3) vol. 79, March 1944, p. 102.

of malaria it was possible to find parasites in the sternal puncture material when they were not found in the peripheral blood. The writer has attempted but failed to verify this; a study of this matter made by army medical authorities (verbal communication) has also given the idea no support. Sternal puncture material rarely if ever shows parasites when a good thick film of the peripheral blood fails to show them.

*The thick film of the peripheral blood properly stained and examined remains the most reliable and generally applicable method of detecting malarial infection, and moreover a negative result will usually rule out an active malarial infection.*

Here however a word of warning is needed. The detection of parasites in the blood, especially if they are few in number, does not necessarily prove that this infection is the cause of the patient's fever and other symptoms. Nowadays many people in many parts of India are harbouring a malarial infection, with parasites present from time to time in blood films, and with fever often absent completely. Such a patient may develop a fever caused by some other infection, and the presence of parasites in the blood may cause the fever to be wrongly attributed to malaria. A recent case seen in this institution well illustrates this point.

A boy was brought to the outpatient department in a state of wild delirium. The blood film was examined then and there, and a few malignant tertian parasites were found; a provisional diagnosis of cerebral malaria was made, and an intravenous injection of quinine was given at once. The boy was admitted to the hospital. The clinical features however were not quite those of cerebral malaria. The white cell count was found to be 25,000, and a lumbar puncture revealed many pus cells and some meningococci which were the cause of the fever and the delirium.

In this case it was the clinical observations of the patient made at the bedside which aroused the suspicion that the malarial infection, revealed by the blood examination, was not the cause of the symptoms, although the truth of this suspicion was confirmed by laboratory findings. Sound clinical observations will prevent many mistakes. Laboratory findings need interpretation in the light of clinical observations.

*The early initiation of quinine treatment is of course of vital importance. It has however been suggested that the results of treatment are likely to be better if the patient is allowed to have a few rigors before the treatment is started.* This suggestion was repeated in the report of the League of Nations Commission on the treatment of malaria. With a *P. vivax* infection this may be true though rarely practicable, but with *P. falciparum* infection, particularly fresh infection in relatively non-immunes, such a procedure would be absolutely contra-indicated. Moreover even a patient with a *P. vivax* infection not uncommonly has a *P. falciparum* infection too. Unnecessary delay in instituting treatment is, in the writer's opinion, criminal.

A recent example of this is here quoted.

A patient was recently admitted into a hospital at about 7 o'clock in the evening with a history of severe rigor and high temperature during the day. A blood film was taken immediately on admission, but the patient then had only low fever, and the medical officer thought that he need not examine the blood film or institute treatment until the next morning. By next morning however the patient was dead (for he suddenly collapsed and died in the night), and the blood film taken the previous evening and only now examined revealed a very heavy infection with *P. falciparum*. Quinine treatment given on the previous evening might have saved the patient's life.

Hospitals should have arrangements for examining blood films and instituting treatment at any time of the day or night.

*The dosage of quinine.*—The old days of heroic doses of quinine, 40 or even 60 grains in the day, have gone, or should have gone; moreover nowadays we have not got the supplies of quinine. But in a recently published standard book on therapeutics one found advocated the giving of 30 grains of quinine in one dose just before the rigor was due. How many stomachs would stand this dose, and what use would it be if they did? Some have now gone to the other extreme, and recently medical men have written in the lay press and in the medical press stating that 5 grains of quinine given daily for a few days is sufficient for the treatment of an ordinary case of malaria. It is difficult to understand how any responsible person can hold such views.

Recently the writer saw a death from malignant malaria in a patient so treated. Recently also, in the hospital attached to the School of Tropical Medicine, six cases of fairly mild malaria were experimentally treated with 6 grains of quinine a day for 7 days. In one of the cases the treatment completely failed to control the fever or to make the blood negative. In the remainder of the cases the fever was controlled and the blood became negative after several days, but in all the cases relapse occurred between 10 and 21 days later, clearly indicating that the treatment was quite inadequate. Particularly in times of quinine shortage, an unnecessarily large dosage has to be avoided, and, at present, with limited quinine and practically no synthetic antimalarials available, the writer's practice in Indian patients is as follows: In malaria due to *P. falciparum* 22½ grains is given for 2 days followed by 15 grains for 5 days (the mixture contains 7½ grains in one ounce). In *P. vivax* infection the dosage is 15 grains for 7 days. A smaller dosage than this is considered unsatisfactory, for the incidence of relapse increases markedly, more treatment has to be given, and there is ultimately no saving of quinine. In children and in persons much below normal weight, the dosage of drugs may be reduced, but *not in proportion to the body-weight*. In young children, malaria tends to be severe owing to lack of acquired immunity.



and it is inadvisable to take risks from inadequate dosage; moreover children tolerate quinine quite well.

*Methods of administration.*—There is the old question of oral administration versus administration by injection. The advice generally given by most experienced workers is very sound; administration should be oral if possible; only if this is impossible, because the patient is vomiting or is unconscious, should injection be used, and intravenous injection if properly given is the best. But many doctors fear intravenous injections and think that they are unsafe. They are however perfectly safe provided that the dosage is not too big, not exceeding 10 grains in heavily-built men (in most Indians 6 or 7 grains is usually adequate), and if the injection is given very slowly taking at least 10 minutes, timed by the watch. The writer recently saw a report of 500 consecutive intravenous injections without any accident.

Then there is the mistaken idea that even if the patient remains comatose or persistently vomiting, not more than 10 grains of quinine should be given in a day by the intravenous route. This opinion was actually quoted in a recent case report in the *Lancet*. The patient died. It is true that in many cases one injection is sufficient to make oral administration possible, but a second and very occasionally even a third intravenous injection may have to be given in 24 hours,\* and possibly repeated later, but the interval between injections should usually be at least six hours.

There remains the question of intramuscular injection. There is still widespread among doctors, and also among the general public possibly encouraged by certain doctors, the idea that quinine given by injection is more rapidly effective than an equal amount of quinine given by the mouth. The only available report of a study of this matter was made by McLay (1922) during the last war. McLay found that quinine given by intramuscular injection actually caused a slower decline in the fever and took a longer time to make the peripheral blood negative than an equal amount of quinine given for an equal number of days by mouth. Moreover, after oral administration, quinine appeared more rapidly in the urine, showing that it was more rapidly absorbed than after intramuscular injection. A study of this matter is now going on in the School of Tropical Medicine, and the preliminary findings are that intramuscular quinine is little if any more effective in controlling the fever and in making the blood negative than the same dosage given by the mouth.

Nevertheless some practitioners still habitually give quinine by injection even to patients who can easily take it by the mouth. One hesitates

to make harsh judgments, but it appears that a potent reason may be that a doctor can get a bigger fee for giving an injection than for prescribing a quinine mixture or tablets.

It is not that intramuscular injections of quinine are never justified. The writer has given them himself to small children with severe malaria with vomiting and convulsions, because it was impossible to get and keep the needle in a vein for the necessary time for an intravenous injection, but such occasions are not common. This is the main use of intramuscular injection, in very young children in whom either oral administration or intravenous administration is difficult or impossible.

A recently issued army instruction regarding intramuscular injection of quinine might here be quoted. 'Dangerous sequelae may occur; absorption is slower than by the oral route. This method of administering quinine is now almost universally condemned and must not be used.'

The *Indian Medical Gazette* has in the last few months in its correspondence columns published two simple methods of turning quinine sulphate into quinine hydrochloride suitable for injection; if these methods have in view the occasional case of malaria which needs injection treatment, no objection can be raised, but if it is implied that intramuscular injection is the best method of treating malaria in general, one must protest and protest very strongly. A leading article with this implication recently appeared in the *Statesman*, Calcutta.

*Other 'specifics' for malaria.*—Finally we come to the substitute 'specifics for malaria of all kinds' which are sometimes 'more effective than quinine or atabrin' the advertisements of which now fill the lay press and sometimes appear in medical journals; needless to say the advertisements are grossly misleading. (This matter is discussed in an editorial in this number.) Individuals and firms are exploiting the present shortage of antimalarial remedies, are filling their own pockets, but incidentally may be causing prolonged sickness or even death of persons who, deceived by these advertisements, are not getting good antimalarial drugs even when they are available. The matter is a public scandal, and we hope that before long this evil may be controlled.

There is no substitute for the genuine antimalarial drugs, quinine in its various forms, and atabrin under its various names (mepacrin, quinacrin, etc.). Other drugs have some antimalarial action, arsenic, some of the sulphonamides, the amorphous alkaloids of cinchona, but this action is limited and in any case is not sufficient to justify their general and indiscriminate use in malaria: in fact, such a use is definitely dangerous.

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\*The reader's attention is drawn to the case reported by Duffy in this issue of the journal (p. 211) in which quinine was given intravenously every 4 hours with a total dosage of 76 grains in 40 hours.—EDITOR.

# REPORT OF A CASE OF CEREBRAL MALARIA

By C. A. GAVAN DUFFY, M.D., M.R.C.P.  
MAJOR, R.A.M.C.

16th October, 1943.—Following a few days' fever, the patient, a sepoy aged 25 years, was admitted unconscious at 8.30 a.m. It seems that he had been unconscious for some hours, and had had no previous treatment. Serial slides were examined, and intravenous quinine was given until the blood ceased to show any rings, as follows :—

Time	Quinine (intravenous), grains	Thick drop M.T. rings per field	Remarks
9 a.m.	10	20	
1 p.m.	6	..	
5 p.m.	6	50	
9-30 p.m.	6	..	
17-10-43			
2-30 a.m.	12	..	Lumbar puncture. C.S.F. pressure 130 mm. water.
7 a.m.	6	15	
1 p.m.	6	..	Strabismus. Bilateral extensor plantars.
3-30 p.m.	6	5	Bilateral ankle-clonus.
7 p.m.	6	..	
11 p.m.	6	0-2	
18-10-43			
1 a.m.	6	..	Able to swallow.
10 a.m.	..	0	
12-30 p.m.	6	..	Lumbar puncture. C.S.F. pressure 110 mm. water. Slight pulmonary involvement.
19-10-43			
10 a.m.	Pamaquin	0	Follows one with his eyes occasionally.
20-10-43			
10 a.m.	"	0	Follows one with his eyes constantly.
21-10-43			
10-a.m.	"	0	Quite conscious. Talks rationally. C.N.S. normal.

He had quinine intravenously, 46 grains during the first 24 hours, and 30 grains during the next 16 hours, i.e., 76 grains in 40 hours, or almost 2 grains an hour. Ten minutes were allowed for each injection of 6 grains.

He was able to swallow fluid after 40 hours, but was unable to speak and did not move until the morning of the sixth day. His subsequent progress was uneventful and he has returned to duty.

It is to be noted that the second slide, 8 hours after treatment had begun, showed a heavier infection than the first one.

The first slide showed two crescents per field, and, while the quinine was being given and

the rings being destroyed, the number of crescents steadily increased to fourteen per field. Pamaquin was then given, and in four days the slide was quite clear.

Lumbar puncture, towards the end of the first 24 hours and again during the third day, showed that the C.S.F. was under normal pressure, so that in this instance there was no cedema of the brain. The fundi were normal.

The long period during which the patient remained unconscious and the abnormal neurological signs on the second day suggest that, had treatment been more leisurely, recovery would not have taken place.

The rectal temperature remained 102°F. to 103°F. during the period of unconsciousness, five days, due in part, during the last two days, to pulmonary involvement for which M&B 693 was given, at first intravenously and later by mouth.

Adequate intravenous glucose-saline was given until he was able to swallow.

## Commentary

Many medical men give quite inadequate quantities of quinine when the intravenous route is required for cerebral malaria. Some have been taught that they must never use it. This case demonstrates that at least one man has tolerated 76 grains in 40 hours, and a number of other patients with less severe attacks have had 36 grains in 24 hours.

It is important to destroy the organisms as early as possible, if one is going to prevent death from cerebral damage or hypostatic pneumonia. As experimental work seems to show that intravenous quinine remains in the circulation for but a short time, it seems clear that it must be repeated frequently and, provided it be given slowly, it is quite safe to do so. If 10 minutes are allowed for 6 grains it is not necessary to dilute the quinine, nor is there any need to add adrenalin. To give an injection slowly it is necessary to have a chair—and a watch.

May I suggest that, for the treatment of cerebral malaria, an excellent set of rules would be—

Serial slides should be examined, and the organisms per field counted to estimate progress. The standard thick drop is sufficiently accurate.

Intravenous quinine, grains 6 should be given at once, again one hour later, and then *four-hourly* until the slide is clear.

Each injection of grains 6 should take 10 minutes. If the doctor can't afford the time, he should not be treating such a serious disease.

The C.S.F. pressure should be measured, and, if raised, brought down to normal.

The usual care of an unconscious patient is required—sufficient fluid, intravenous, if necessary (the quinine may be added to it), avoidance of pneumonia by propping up (M&B 693 may be necessary) and avoidance of bladder distension.

## PREFRONTAL LEUCOTOMY IN SCHIZOPHRENIA WITH REPORT OF 25 CASES

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and

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IN view of the rather discouraging results and relapses with shock therapy with insulin (Sakel, 1934), with cardiazol (Meduna, 1937), with electrical convulsions (Cerletti and Bini), in the treatment of schizophrenia and other allied mental disorders, and in view of the hopeless ultimate prognosis of such cases, more drastic methods seem justified, where other methods of treatment are either unsuitable or have failed. It is from this viewpoint that the operation of *prefrontal leucotomy* first recommended and performed by Moniz in 1936 seems justified, and any improvement in the condition of the patient constitutes a progress in the treatment of mental diseases. The published results of U.S.A. and Great Britain, where the operation is rapidly gaining support, offer a hope of cure where the other accepted methods of treatment are unsuitable or have failed.

This operation was first performed at the Government Mental Hospital, Bangalore City, Mysore State, S. India, on 21st September, 1942, and this paper deals with the technique, experience and results of 25 cases operated on by us till October 1943. A detailed psychiatric analysis of this series is under publication, and this paper deals mainly with the surgical aspects.

Moniz's original technique has been modified by numerous workers, notably by Lyster (1938), and by Freeman and Watts (1939) who use a lateral approach. The operation is based on the assumption that the frontal lobe is producing a disordered note in the smooth working of the 'intellectual' behaviour of the person, and that by isolating the frontal cortex from the rest of the brain, a 'release' of the other parts of the cerebral hemispheres occurs. This isolation is best attained by cutting the subcortical white matter as it lies in front of the anterior horn of the lateral ventricle. Moniz approached this area by trephine holes from the superior aspect of the skull, crushed the white matter with an expanding wire, and injected alcohol to make sure that most of the white matter had been interrupted. Freeman and Watts in 1939 modified the technique by approaching the frontal lobe from the lateral aspect of the skull; the white matter being severed by a nasal elevator. McGregor and Crumie (1941) devised an instrument so adjusted as to cut a core of white matter  $2\frac{1}{2}$  cm. in diameter.

Lyster, using a lateral approach similar to that recommended by Freeman and Watts, turned down a flap of bone and exposed the brain. After the introduction of a brain speculum, the white matter is severed under direct vision. This open method is fundamentally sound, and is very attractive to all who hate a blind procedure; it has the disadvantage of being a very formidable operation. The Freeman-Watts technique, as followed by us, is simple and relatively safe. Both our experience and that of others following a similar procedure have indicated no serious disadvantages, and we do not feel justified in submitting our patients to the more severe Lyster operation with its correspondingly increased risks.

In our series we have used the lateral approach as suggested by Freeman and Watts, and in the first ten cases used a Killian's nasal elevator to cut the white matter; in the later cases we used a modified McGregor and Crumie leucotome.

### Technique

The technique followed by us is practically similar to that recommended by Freeman and Watts. The pre-operative preparation consists of giving an ounce of castor oil as a cathartic on the day previous to the operation, followed by an enema on the morning of the operation. The head is completely shaved in men, but in women, only that portion of the scalp which is anterior to a line joining the two external acoustic meatus over the vertex. Premedication with one capsule of sodium amytal is given if the patients are very apprehensive or very violent. In the more quiet type of patient, no premedication is resorted to.

The patient is laid flat on the table with the head slightly raised on a pillow.

*Anæsthesia.*—Whilst many American workers have used local anæsthesia, we find it difficult to use local anæsthesia alone, especially in the agitated and violent type of patient. Various rectal and intravenous narcotics have been used in Great Britain and Europe, but our choice has been pure chloroform given by the open method both for induction and maintenance. We have noticed no ill-effects from this agent, provided that ordinary precautions are taken, and all the cases in this series have been operated upon under open chloroform anæsthesia.

After sterilizing the skin with tincture of iodine, towels are draped, and a point 3 cm. behind the curving lateral orbital margin and 5 cm. above the zygoma is marked on the skin. Latterly, however, we have found that a point  $2\frac{1}{2}$  cm. behind the anterior orbital margin and  $5\frac{1}{2}$  cm. above the zygoma is more suitable, as with the measurements recommended by Freeman and Watts, we often found ourselves confronted with the anterior branch of the middle meningeal artery at the site of the trephine or burr hole. To facilitate easy measurements of the desired point, a localizing

plate (shown in figure 2) is used. The opening in the plate is situated 3 cm. from one edge and 5 cm. from the other edge. The shorter side lies on the zygoma and the longer against the orbital margin, and the hole corresponds to the site of the burr hole. After the point on the skin has been marked, an incision is made 4 cm. long, equally placed above and below the point, in the direction of the fibres of the temporalis muscle. The incision is entirely within the hair margin. The incision is deepened to the bone and, with a rugine, the muscle and the temporalis fascia covering it are detached from the bone and retracted firmly with a self-retaining mastoid retractor to give a wide exposure and a bloodless field. The coronal suture can occasionally be seen, but in our experience it is not often possible to identify the suture at this point, and consequently it is of little help. Where the suture could be identified, the burr hole was always placed anterior to it.

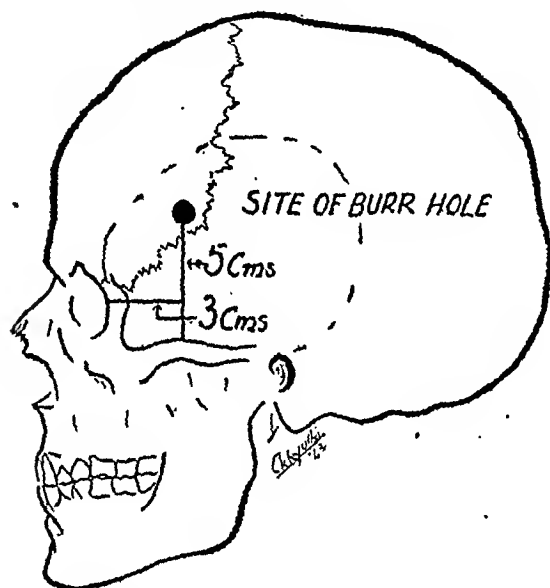


Fig. 1.—Showing site of burr hole.

In our first 9 cases, a trephine opening 2 cm. in diameter was made (the disc being replaced at the end of the operation), but in the later cases, a burr hole  $\frac{1}{4}$  cm. in diameter was made with a Carr's burr. The bleeding from the diploë of the skull is stopped with cotton pledgets soaked in warm saline or in Horsley's wax. A similar opening is made on the opposite side. The head is now steadied, with the face looking vertically upwards towards the ceiling. The width of the brain from one dura to the opposite side is measured with a caliper. We have found very little variation in the width, the maximum in our series being 11.5 cm., the minimum 9.5 cm. and the average has been  $10\frac{3}{4}$  cm. From this, the width of the white matter is estimated, and the stop on the instrument is arranged so as to adjust the depth to which the instrument is to be introduced without injuring the grey matter on the medial surface of the prefrontal cortex.

An avascular area of the dura is chosen, and a triradiate incision is made with a Von Grafe cataract knife after lifting the dura from the underlying brain with a dural hook, and the subarachnoid space is opened. A small quantity of cerebrospinal fluid usually escapes, though in some cases as much as 3 ounces of fluid was lost on each side. (This is of no consequence.) A needle with a stylette is introduced to the calculated depth in the direction of the opposite trephine opening, the stylette is withdrawn, and suction is applied with a syringe so as to make sure that the needle has not entered the anterior horn of the lateral ventricle. If cerebrospinal fluid is aspirated, the needle is withdrawn and reintroduced in a slightly more anterior direction; if no fluid is encountered, a Killian's blunt nasal elevator is introduced alongside the needle, to the calculated depth, and the needle is withdrawn. The elevator is now moved through an arc of  $60^\circ$  with the dura as the centre of the arc, and in the plane of the coronal suture. The elevator is withdrawn, and it is surprising how little bleeding follows this procedure. The slight amount of bleeding that usually occurs is easily controlled with warm saline irrigation.

A wet saline gauze pack is left in the wound, while the same procedure is repeated on the opposite side. The dura is difficult to suture on account of the small size of the burr hole, and is left unsutured; this is of no disadvantage. The wound is closed in layers without drainage.

This technique recommended by Freeman and Watts was followed by us in the first ten cases. In the later cases, the severing of the white matter was done with a modified McArthur and Crumbie leucotome.

This instrument consists of a rotating blade controlled by a screw device. Combined with it the instrument is made hollow so that suction can be applied to make sure that the instrument has not entered the anterior horn of the lateral ventricle, thereby dispensing with the passing of a needle to test the extent of the anterior horn of the lateral ventricle and so combining both manœuvres of testing and cutting in one.

We have found no difference either in the amount of hæmorrhage or in the after results by the different methods. The use of the McArthur and Crumbie leucotome simplifies the procedure. The instrument has an adjustable stop so as to control the depth to which the instrument could be introduced after estimating the width of the white matter so that the medial surface of the prefrontal cortex is not damaged. In our experience, the mark 4 on the leucotome usually answers the purpose well in most cases. The blade cuts a core  $2\frac{1}{2}$  cm. in diameter, and the instrument is introduced in the same manner as the nasal elevator described above, the stop abutting against the dura, and the plane of movement of the blade corresponding to the plane of the coronal suture.

After the wound has been sutured in layers without drainage, the wound is dressed and

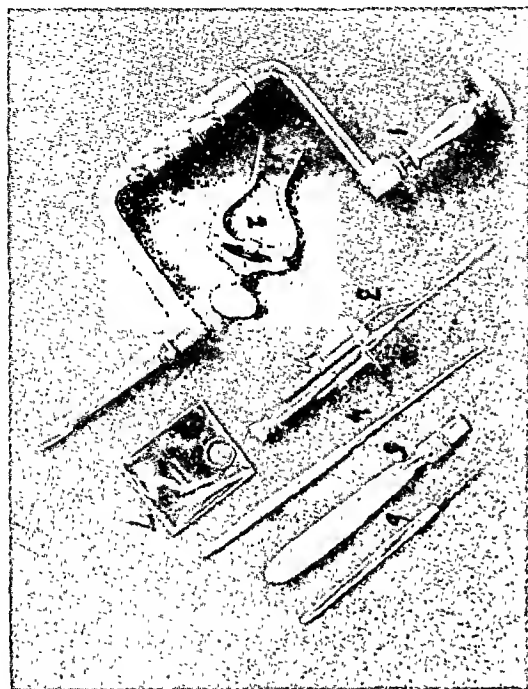


Fig. 2.—Showing the special instruments used.—

1. Burr.
2. Retractor.
3. Leucotome.
4. Dural hook.
5. Rugine.
6. Cataract knife.
7. Localizing plate.

bandaged, and the patient is returned to the wards. After he has regained consciousness, he is supported in bed with a back rest, and fluids are given freely by mouth.

Certain changes in the condition of the patient are noted as the white matter is cut with the leucotome. When the blade is rotated nearly completely, the respiration, which has been up to now regular, suddenly becomes irregular both in rhythm and depth. Often short gasps are followed by a long sighing type of respiration. In some, the respiration has become very shallow and occasionally stopped. These disturbances of respiration occur suddenly as most of the fibres of the frontal lobe are cut. Where respiration has failed, artificial respiration for a few minutes has always brought the respiration back to normal rhythm and depth. Sectioning the white matter on the opposite side has produced a second similar disturbance, but usually less marked.

Simultaneously with the respiratory disturbances, the pulse becomes irregular for a few beats and sometimes becomes thready and imperceptible. In no case of our series has the heart completely stopped beating, and the cardiovascular changes are very transient and are probably secondary to the respiratory

embarrassment; they recover earlier than the respiratory changes.

The sudden change when the white matter is sectioned in a patient whose breathing is regular, and a similar change seen, when the opposite prefrontal white matter is cut, strongly suggest that some controlling influence from the prefrontal cortex to the respiratory centre either directly or through the medium of other centres has been suddenly interrupted, thereby throwing the respiratory centre 'out of gear' momentarily. During the period of readjustment, the respirations become irregular. The cardiovascular irregularity is probably caused by an irregular overflow of impulses from the respiratory to the cardiovascular centre in the neighbourhood.

Little or no post-operative attention is necessary. Patients are seldom restless but some are drowsy. Where they tend to be restless, or complain of severe headache, morphia  $\frac{1}{4}$  gr. with atropine  $\frac{1}{100}$  gr. is given intramuscularly and repeated if necessary. The post-operative period in our series has been singularly free from symptoms. Retention of urine was seldom seen in our series, and, in three of our cases, incontinence and bed-wetting lasting from one to six days was complained of; all recovered normal micturition after the first week. Headache, which in some was severe, usually disappeared by the second or third post-operative day. The slight rise of temperature on the second post-operative day usually subsides in twenty-four hours, and the pulse rate was not raised unduly. The sutures were removed on the tenth post-operative day and the bandage discarded two days later.

One of the striking features in the post-operative period has been the increased appetite. During the period in hospital after operation, there was a uniform increase in weight in all the patients. This gain in weight could not have been ascribed to any special diet, rest, or nursing, as such increase was not observed after cardiazol or insulin shock therapy, even though in the post-shock therapy period, the care of the patients, diet and nursing were practically the same as during the post-operative period. On the psychological side, in many, if not all, there is a profound change, even from the day of the operation. Patients who were violent are subdued, the bellicose are more modest; they have lost their hallucinations, take a more intelligent interest in the surroundings and in conversation, the voices that used to talk to them are no longer heard, and the patients appeared to be calm and placid. This improvement has been progressive and maintained.

#### *Rationale of operation*

Moniz, in discussing the theory which led him to propose prefrontal leucotomy, considers that in normal people functional connections between the cortical cells are variable, giving various combinations of groupings. In certain mental



disorders, these groupings become fixed instead of being variable, and give rise to obsessions and delusions. He argued that, if these pathways are disconnected, the obsessions and delusions would disappear.

Experimental evidence on chimpanzees has shown that the removal of the frontal areas gives rise to some form of deficiency that has been termed 'intellectual'. Extirpation of the frontal lobe either as a result of accident (American crowbar case) or by deliberate surgery (Brickner's 1939 and Ackerley's 1935 cases) has shown slowness, deliberate activity, perseverance and freedom from anxiety on the part of the patient after the extirpation. Bianchi concluded that prefrontal lobe damage in monkeys tends to disaggregate the personality, and incapacitate the serializing and synthesizing groups of representations. Franz summarized the deficits in cats and monkeys in terms of deterioration of recently formed habits.

To quote Moniz: 'the idea was to operate upon the brains of patients, not directly upon the cell groups of the cortex or of other regions, but rather by interrupting the connecting fibres between the cells of the prefrontal area and other regions, that is to say, by sectioning the subcortical white matter'.

The frontal lobes form the latest stage in the evolution of the brain, but no definite conclusions as to their function have been arrived at so far. With refinement and specialization of the motor functions, the frontal lobes have attained a large size in anthropoids and a truly extraordinary size in man, in whom associational processes (figure 3) have reached a higher level. The superior longitudinal fasciculus is a bundle of great importance highly developed in the human brain.

Observations made of patients before and after frontal lobectomy by Ackerley for a tumor of the frontal lobe, and by Brickner (1939) who has performed it bilaterally, have suggested that the frontal lobe had a synthesizing function and enables us to become aware of an increasing number of simultaneous impressions. After removal of the frontal lobe, to quote Ackerley, 'we cannot but be impressed with the effortlessness with which the person is living'. According to Freeman and Watts (1939) the essential part of the prefrontal leucotomy is the division of connections between the frontal lobes and the thalamus.

### Complications

Various complications of the operation have been mentioned by different authors. Many of these are transient, but some are of a permanent character. In our series, we have met with no serious complications, and none of a permanent

character. Haemorrhage either at operation or soon after, is one of the most serious, and has been responsible for the majority of fatalities of the operation. Incontinence of urine, particularly bed-wetting during sleep, is fairly common, but most patients recover normal control in a few months. Various ocular changes have been mentioned. They include sluggish pupils, anisocoria, Argyll-Robertson pupils, myosis, ptosis, nystagmus, etc. We have noticed no such pupillary changes in our series. Somnolence for one to two days, mild pyrexia lasting four to five days are some of the mild post-operative phenomena observed. More severe, and producing mental deterioration, are epileptic convulsions, restlessness and violence, trismus and fibrillary contractions of the platysma and masseter muscles. These are of grave import and probably terminate fatally. Various degrees of residual paralysis, from aphasia to monoplegia and hemiplegia and sphincter disturbances associated with diarrhoea, have been reported in the literature. Though a formidable list of complications has been given, it is our impression that, excepting haemorrhage, the other complications are either trivial or transient, and that the more serious ones are seldom seen; but no definite conclusion can be drawn from such a short series regarding the incidence of the various complications.

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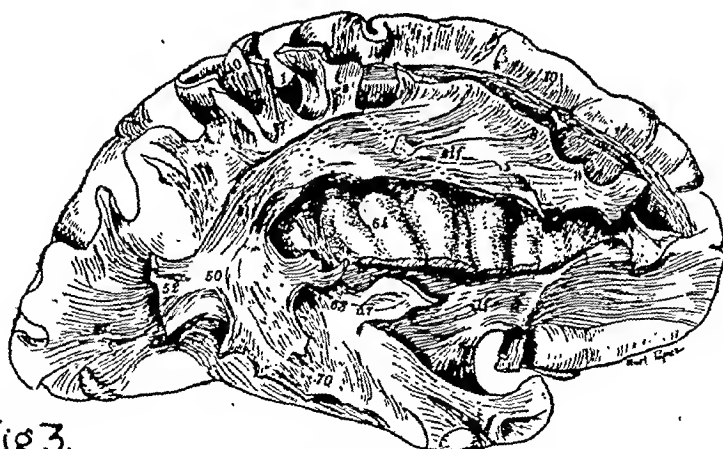


Fig 3.

Association bundles in the human brain,  $\times 1$ . *slf*, superior longitudinal fasciculus; *ilf*, inferior longitudinal fasciculus; *or*, optic radiations; *ar*, auditory radiations.

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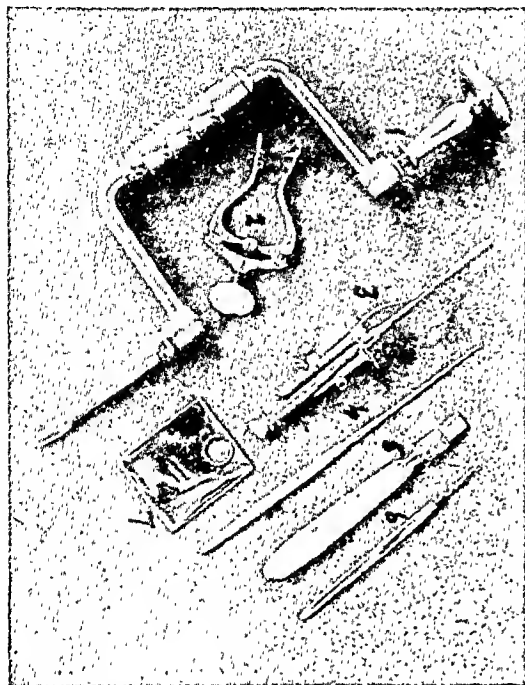


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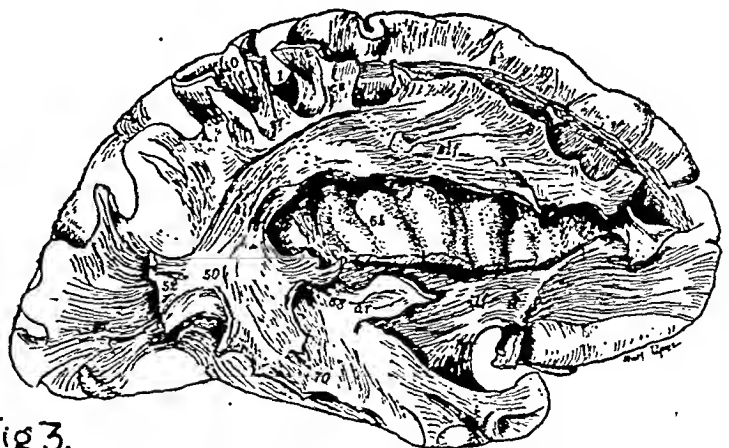


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The accompanying table shows the type of cases operated on and their clinical and post-operative histories.

TABLE

Case	Sex	Age	Occupation	Diagnosis	Date of operation	Mental state before leucotomy	Previous treatment	Results of operation
1	M.	27	Farmer	Schizophrenia 7 years.	21-9-42	Noisy, violent, destructive with auditory hallucinations.	Cardiazol in 1940 with no effect.	Well behaved, quiet, recovered.
2	M.	30	Labourer	Schizophrenia paranoid duration more than 6 years.	23-9-42	Violent, boisterous, destructive with offensive habits. Auditory and visual hallucinations and disconnections.	Ammonium chloride and cardiazol with no benefit.	Easily manageable, quiet, but his delusions and disconnections persist.
3	M.	35	Cook	Schizophrenia 5 years.	11-10-42	Morbidly preoccupied, dull and depressed with spells of acute excitement.	Ammonium chloride and cardiazol without benefit.	Became bright and cheerful immediately after operation. Is able to attend to work where no special skill is required.
4	M.	34	Compounder	Schizophrenia	12-10-42	Hallucinations, delusions and disconnections with marked deterioration and vagrancy.	Ammonium chloride in 1941. Without benefit.	No improvement.
5	M.	30	Farmer	Schizophrenia paranoid 5 years.	15-11-42	Violent, boisterous with disconnections, automatisms, offensive habits and signs of deterioration.	Nil	No improvement.
6	M.	35	Petty merchant	Schizophrenia paranoid 4 years.	16-11-42	Mischievous and fixed delusions of grandeur.	Nil	Is quiet and manageable.
7	M.	35	Clerk	Schizophrenia paranoid (dementia praecox) 7 years.	30-12-42	Poor heredity. Brothers schizophrenics. Hallucinations, auditory visual delusions of grandeur and persecution, disconnections, automatisms.	Cardiazol and ammonium chloride in 1941 without benefit.	Is passive, has no initiative, is clean and obeys instructions mechanically.
8	M.	30	Labourer	Affective disorder c Schizophrenia features 5 years.	31-12-42	Patient violent, boisterous, offensive habits, auditory hallucinations with delusions of grandeur with spells of blankness and depression.	Ammonium chloride and insulin. No benefit.	Not violent, and is manageable.
9	M.	32	Clerk	Schizophrenia paranoid 7 years.	28-1-43	Bad heredity. Two sisters schizophrenics. Disconnected, filthy, deteriorated with meaningless laughter and excitement.	Cardiazol. No benefit.	Died of broncho-pneumonia on 2-3-43 after a perfectly normal convalescence.
10	M.	26	Cook	Schizophrenia paranoid 3 years.	29-1-43	Depressed, morbidly preoccupied, auditory and visual hallucinations, with spells of excitement, fleeting delusions.	Cardiazol and ammonium chloride without benefit.	Improvement almost immediately after operation. Worked in the hospital kitchen. Discharged, recovered on 7-8-43.
11	M.	..	Clerk	Schizophrenia paranoid 6 years.	26-2-43	Disconnected meaningless talk, garrulity, delusions of grandeur, auditory hallucinations with signs of deterioration.	Cardiazol without benefit.	Overproductive and disconnected in talk, but otherwise harmless.
12	M.	24	Student (high school).	Schizophrenia paranoid 3 years.	25-3-43	Violent, assaultive, dirty in habits, delusions of persecution. Homicidal assaults. Visual and auditory hallucinations.	Ammonium chloride, insulin and cardiazol without benefit.	Consciousness clear and well oriented. Lost all initiative. General deterioration of intelligence.
13	F.	25	Housewife	Schizophrenia catatonic 3 years.	26-3-43	Morbid preoccupations, violent, meaningless excitement, offensive habits. Catatonic episodes.	Cardiazol and insulin without benefit.	Recovery spectacular from third day of operation. Improvement maintained. Looking after children and efficiently managing a difficult household.

14	F.	30	Housewife	6 years.	26-3-43	Poor heredity. Mother and brother are manic depressives. Deteriorated. Overproductive disconnected talk, theatrical and grandiose behaviour with delusions of grandeur and spells of meaningless excitement. Intelligent, restless, noisy, disconnected and deteriorated.	Shock therapy of no benefit. Cardiazol without benefit.	No improvement. Well behaved, talks sensibly, but still slightly overproductive.
15	M.	30	Schoolmaster	Schizophrenia paranoid 3 years.	22-5-43	Spells of meaningless excitement. Intelligent, restless, noisy, disconnected and deteriorated.	Cardiazol and insulin without benefit. Cardiazol with some improvement. It was followed by a breakdown.	Dull and depressed, is morbidly occupied and has lost all initiative. No improvement, remains dull and depressed.
16	F.	33	Housewife	Schizophrenia paranoid.	23-5-43	Poor heredity. Father manic depressive, mother backward. Acute schizophrenic episodes all after child birth. Lignature of fallopian tubes 2 years ago.	Ammonium chloride and cardiazol without benefit.	Quiet and co-operative. Reported to be attending to her household tasks without difficulty. Recovered.
17	F.	30	Housewife	Schizophrenia over 6 years.	23-5-43	Illiterate, dull and dazed, dirty habits, automatisms, childish behaviour with spells of meaningless excitement. Restless, offensive habits, automatisms, with delusions of persecutions and spells of excitement.	Cardiazol without benefit.	Quiet, clean and inoffensive. Talks generally, rationally, but at times silly and childish.
18	F.	25	Agriculturist	Schizophrenia simple 5 years.	19-6-43	Restless, noisy, assaultive with delusions of grandeur and 'disconnections'.	Ammonium chloride, cardiazol and insulin without benefit.	Quiet, well behaved, rational in ordinary conversation, grandiose ideas have disappeared.
19	M.	32	Student	Schizophrenia paranoid 7 years.	21-6-43	Honours graduate. Very intelligent. Restless, exhibitionist and theatrical with delusions of grandeur and fits of meaningless excitement.	Insulin and cardiazol without benefit.	Well behaved. Has gone back to her ordinary social and household duties.
20	M.	35	Engineer	Schizophrenia 4 years.	21-6-43	Restless and interfering. Fleeting delusions of grandeur and meaningless excitement. History of homicidal assaults against his wife and his father.	Ammonium chloride, insulin and cardiazol without benefit.	Pleasant, well behaved, and no fits of violence. Still under observation.
21	F.	31	Housewife	Schizophrenia paranoid 4 years.	23-7-43	Asthenic, anxious, agitated with spells of acute panicky excitement, ideas of persecution and self-reproach, agitated depression.	Insulin and cardiazol without benefit.	Quiet, well behaved and seems to have recovered from his psychotic episode.
22	M.	28	College student	Schizophrenia 6 years.	24-7-43	Restless, shouting and singing to himself, never violent or assaultive, fleeting delusions of grandeur, disconnections prominent.	..	Friendly and co-operative. Works hard in the hospital kitchen.
23	M.	28	Engineer	? 3 years.	17-9-43	Poor heredity. Present attack is the third of three acute schizophrenic episodes characterized by intense restlessness, hilarity excitement, vandalism, auditory and visual hallucinations.	Insulin and cardiazol without benefit.	Spectacular improvement almost immediately after the operation.
24	M.	34	Farmer	Schizophrenia simplex 6 years.	18-9-43			
25	M.	22	Student	Schizophrenia 3 years.	22-10-43			

*Mortality*

One of the encouraging features of the published literature is the low mortality associated with this operation. Freeman in 31 cases

trolling hæmorrhage after leucotomy with the McGregor and Crumbe leucotome. No comparative figures of mortality in Indian patients could be obtained, as we are not aware of any

*Summary of results*

Men	Women	Total number	Recovered	Improved	No change	Deteriorated	Mortality
19	6	25	7	6	10	2	Nil

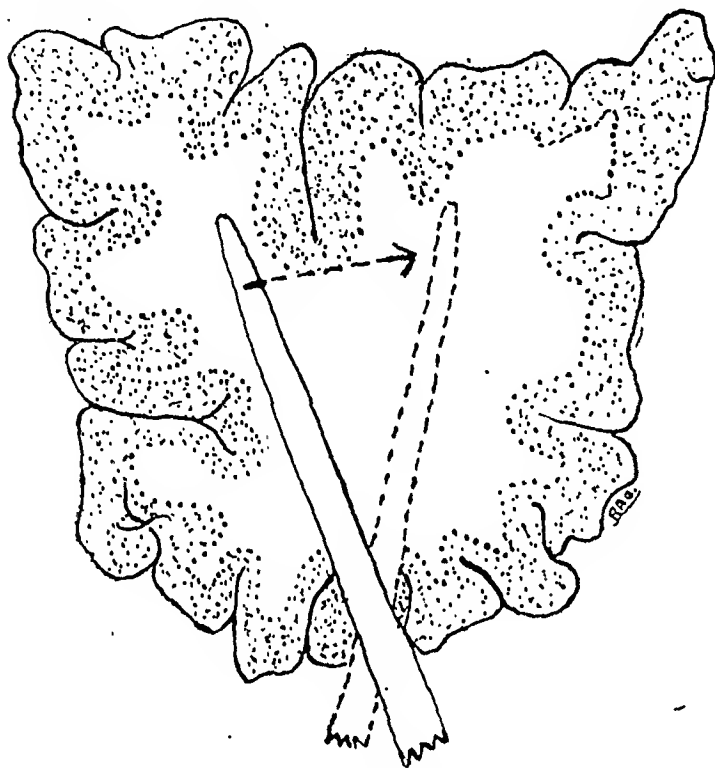


Fig. 4.—Showing the source of hæmorrhage from a vessel lying deeply in a sulcus.

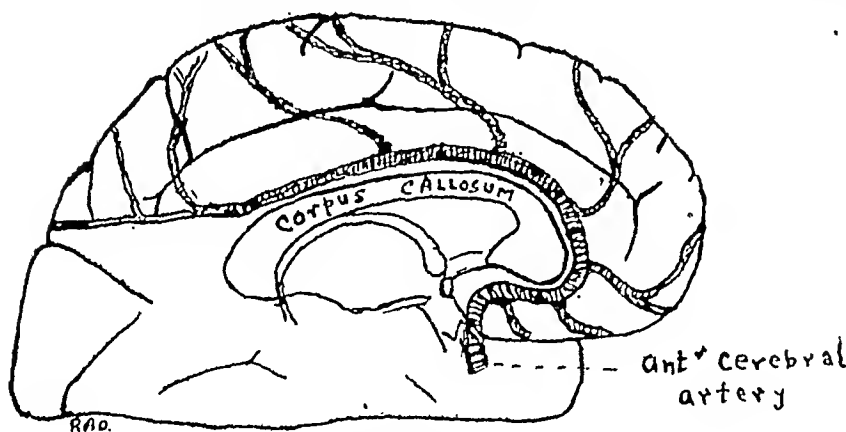


Fig. 5.—Diagrammatic representation of the anterior cerebral artery with branches.

had 3 deaths; Rizatti and Borgarello had no deaths in a series of 185 cases; Dax and Smith (1943) had 2 deaths in 50 cases. Most of the cases have died within three to four days of the operation, due to hæmorrhage. We have had no mortality so far in our series of 25 cases, although in three cases we had an anxious time in con-

published reports of similar work from any source in India.

We have classified those patients who are able to adjust themselves to their home surroundings, carry on their normal work as efficiently as could be expected of them, as 'recovered'; as 'improved' those who are friendly and co-operative, clean in their habits and able to look after themselves. In the two deteriorated cases it is difficult to state whether the operation had anything to do with the deterioration, or whether they would have deteriorated in any case. In this series the longest duration has been seven years and the shortest three years; this should only be taken as approximate, for in many cases the history is unreliable, or the patients and relatives might not have noticed slight symptoms of longer duration. In all these cases, however, the period of observation is too short to assess accurately the final results of the operation.

*Selection of cases*

All the cases in our series, consisting of 19 men and 6 women, were physically good operative risks, the youngest being 22 years and the oldest 35 years of age. In many of these cases, shock therapy had failed to give any relief. All of them had been ill for several years, and the majority of them were schizophrenics; in a few, schizophrenic syndromes had been superimposed on a primarily affective disorder. We have as yet formed no definite conclusions as to the most suitable type of case for leucotomy, but we feel that the chances of recovery are greater in the more 'intellectual' type of patient, though statistical proof for this is lacking.

When to operate on a patient is still a moot point. Although favourable results have been reported in cases of five to twelve years' duration, the general feeling has been tending towards earlier surgical treatment. We do not feel justified in dogmatizing as to the time most suitable for operation, in view of the fact that

at best, it is an operation of mutilation, in which a portion of the brain is completely isolated functionally from the rest of the brain. But in view of the progressive deterioration of the patient, it seems that the operation is justified when other less radical methods have been given a reasonable trial and found to have failed. When once it has been decided that other methods of treatment have failed, we feel strongly that earlier operation has undoubtedly a much better chance of success. We believe that prefrontal leucotomy is indicated when the mental disorder has failed to respond to other methods of treatment, and where the prospects of spontaneous recovery are remote.

### Conclusions

The encouraging results obtained in a short series of 25 cases with a poor prognosis make us hopeful of this useful method of treatment. While no theoretical support can be brought forward yet to justify the rationale of the operation, the favourable results obtained by us in India and by others abroad justify further investigations of the functions of the frontal lobe, and of methods of obtaining better insight into the pathological processes and the biochemical changes in these mental disorders. Numerous criticisms of this operation have been made, some on humanitarian grounds and some on the grounds that a more serious disorder has been inflicted on the patient than he is already suffering from. The modern concept of brain physiology and function is essentially dynamic, and we might agree with Golla (1943) that 'one need not be nervous in undertaking this procedure for fear of producing permanent mutilations in the brain'.

### Summary

(1) Bilateral prefrontal leucotomy has been performed on 25 patients at the Government Mental Hospital, Bangalore, Mysore State.

(2) The technique followed by us is described.

(3) Short case reports and results are tabulated.

(4) The theoretical aspects of the operation and the justification of the operation are discussed.

### Acknowledgments

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# THE QUALITY OF INDIAN-MADE SYNTHETIC DRUGS—I. EXAMINATION OF P-CARBAMIDO-PHENYL-ARSONIC ACID (CARBARSONE)\* OF INDIAN MANUFACTURE

## Laboratory Study

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## Introduction

WITH the rapid advance of chemotherapy, a large number of synthetic drugs have been introduced into modern therapeutics. Until recently, India was almost completely dependent on foreign sources, chiefly Germany, for the supply of almost all her requirements in this direction. This was strikingly manifested by the precipitous rise in prices immediately after the declaration of war against Germany in 1939. Since then the shortage of German-made and other imported synthetics has caused two important results: (1) Indian physicians are gradually showing an increasing conviction in the fact that it is possible to carry on medical aid and rational treatment without many of the imported drugs by using worth-while substitutes of other makers; and (2) those few synthetics which were in great demand are being rapidly replaced by Indian-made drugs. In connection with the second result, progressive Indian commercial concerns have fortunately taken the lead, and, in many cases, State Institutions such as the Biochemical Standardization Laboratory of the Government of India, the School of Tropical Medicine, Calcutta, and the Haffkine Institute, Bombay, have endeavoured to contribute their technical advice and help.

The Biochemical Standardization Laboratory, as the testing centre for drugs intended for the use of the Defence services, has had the unique opportunity of examining during the last 2 years

\* 'Carbarsone', originally manufactured and introduced by Eli Lilly & Co., Indianapolis, U.S.A., is not covered by a U.S. patent and the firm disclaims proprietary rights to the name. Hence this name has been used in the title.

This compound has been synthesized by at least 4 local firms whose products have been tested by the B. S. Laboratory. (1) 'Amibiaron'—B. C. P. W. Ltd.; (2) Carbarsone—Bathgate & Co.; (3) 'Arsambide'—Brahmachari Research Institute; (4) Carbarsone—Indian Research Institute; also by (5) Department of Chemistry, Indian Institute of Science, Bangalore.

a large number of synthetic drugs of Indian manufacture, e.g., carbarsone, entero-vioform, chiniofonum (anti-dysenteric group), chlorbutol, urethane, phenobarbitonum (hypnotic group), mepacrine hydrochloride (antimalarial group), sulpharsphenamine, tryparsamide (anti-syphilitic and allied group), atophan (analgesic group), urea-stibamine and other types of organic antimony compounds (anti-leishmaniasis group), silver proteinate, etc. (astringent group), acriflavine, methyl violet, eosin, etc. (dyes and microscopic stains group), sulphoamides, etc. (anti-bacterial group), nicotinic acid (vitamin group), etc., etc. In view of the number of enquiries regarding the quality of these Indian-made equivalents that are being constantly referred to this laboratory from members of the medical profession and representative medical organizations, it is deemed expedient to publish from time to time the results of an unbiassed examination of these drugs so that the medical profession can form their own opinion as to the value or otherwise of these equivalents. In the present paper, a report on carbarsone, a commonly employed drug in amoebic dysentery, is presented.

Carbarsone belongs to the original series of organic arsenicals prepared and tested by Ehrlich and Berthelm, which on account of its comparatively feeble trypanocidal properties was not given further trials at that time. Reed and his co-workers (1932) tried it in a small series of cases and found it to be comparatively non-toxic in comparison to other organic arsenicals of the type of stovarsol (acetarsol) or tryparsol, and very effective in amoebic infections. In India, Chopra, Sen and Sen (1933) and Chopra and Sen (1934) tried the drug in the Carmichael Hospital for Tropical Diseases and reported satisfactory results. Since then, carbarsone has been popular with the Indian practitioners in the treatment of intestinal amoebiasis.

## Experimental

A. *Chemical analysis.*—In testing chemically carbarsone powder and tablets from the various indigenous sources, the aims were that the local product should be of a degree of purity at least equal to that of the original brand of carbarsone manufactured by Lilly and Company. Consequently, in the chemical work, the Indian product was always examined parallel with the American-made product, authentic samples of the latter being obtained from the Calcutta agents of the Lilly Company.

The following tests recommended in the 'New and Non-official Remedies' (Amer. Med. Assoc., 1937) were carried out.

### I. Identity and purity tests

(i) *Physical characters.*—Carbarsone is a white, almost odourless powder, having a slightly acid taste.

(ii) *Solubility.*—It is slightly soluble in water and in alcohol and nearly insoluble in ether and chloroform.

The water solution yields an acid reaction to litmus paper. It is freely soluble in alkalis and alkaline carbonates.

(iii) *Absence of inorganic arsenates, etc.*—Dissolve 0.50 gm. of carbarsone in 2 c.cm. of ammonia water, dilute to 5 c.cm. with water and add 3 c.cm. of magnesia mixture solution; no precipitate forms within one half hour (absence of inorganic arsenates); allow the solution to stand for some time longer or heat the solution for some time; a precipitate is produced. Add 10 c.cm. of sodium carbonate solution to 1 gm. of carbarsone in a test tube and gently agitate the mixture: a complete solution results in five minutes (solubility in alkalis). Shake 0.5 gm. of carbarsone for five minutes with 10 c.cm. of diluted nitric acid, filter the mixture, and add a few drops of silver nitrate solution to the filtrate: at most only a very slight turbidity is produced within five minutes (limit of chlorides). Transfer 0.4 gm. of carbarsone to a test tube, add 5 c.cm. of 20 per cent sodium hydroxide, stopper with a slotted cork from which is suspended a strip of moist red litmus paper, and heat gently: the litmus paper turns blue (evolution of ammonia).

(iv) *Residue on ignition.*—Incinerate 0.5 gm. of carbarsone: not more than 0.1 per cent residue remains.

(v) *Loss in weight.*—Heat about 0.4 gm., accurately weighed, of carbarsone for twenty-four hours at 80°C.: the loss in weight does not exceed 1.1 per cent.

(vi) *Melting point.*—Carbarsone melts with decomposition at 169°C. to 171°C. (the U.S.P. melting point determination method is to be used).

(vii) *Distinction from acctarsol.*—Transfer 1 gm. of carbarsone to a suitable test tube, dissolve in a solution containing 10 c.cm. of sodium hydroxide solution and 10 c.cm. of water; add 2 gm. of sodium hydrosulphite and warm the mixture to 50°C.: a light yellow precipitate is formed in an excess of sodium hydroxide solution.

## II. Arsenic content

Place about 0.2 gm. of carbarsone accurately weighed in a glass stoppered 200 to 300 c.cm. flask. Add 1 gm. of finely powdered potassium permanganate and 5 c.cm. of diluted sulphuric acid, and allow to stand for ten minutes, rotating the contents of the flask during this time to insure thorough mixing. Cautiously add 10 c.cm. of sulphuric acid in portions of 2 c.cm. rotating

the flask after each addition. When the reaction has ceased, add sufficient hydrogen peroxide to dissolve completely the brown precipitate (about 5 to 7 c.cm.). Towards the end of the reaction the hydrogen peroxide is to be added drop by drop to avoid any great excess. Dilute with 25 c.cm. of distilled water and boil the mixture gently over an asbestos wire gauze for from fifteen to twenty minutes or until the excess of hydrogen peroxide is evaporated. Dilute with 20 c.cm. distilled water and add tenth normal potassium permanganate until the liquid is faintly pink, then discharge the pink colour by the addition of a drop of tenth normal oxalic acid. Cool the mixture, add 2.5 gm. of potassium iodide, stopper the flask tightly, and allow it to stand in a cool dark place for one hour. Then titrate the liberated iodine with tenth normal sodium thiosulphate without the use of starch indicator.\* Make a blank test with the same quantities of the same reagent and correct the assay for the volume of tenth normal sodium thiosulphate used in the blank. Each c.cm. of sodium thiosulphate is equivalent to 0.003746 gm. of arsenic. The arsenic content is from 28.1 to 28.8 per cent.

## III. Nitrogen content

Transfer about 0.5 gm. of carbarsone, accurately weighed, to a 500 c.cm. Kjeldahl flask. Determine the nitrogen content, according to the accepted method (Microkjeldahl method—Pregl's modification). The nitrogen content is not less than 10.7 per cent, nor more than 11 per cent by weight of the sample.

## Carbarsone powder

Altogether five samples of carbarsone (Indian made) were obtained in powder form and one

\*Some experience is required to ascertain the end point of the titration (i.e. disappearance of the yellow colour of iodine and appearance of a faint green colour). It is also important that the titration is finished with a reasonable and moderate speed; otherwise the yellow colour of iodine slowly reappears and an excess of  $\text{Na}_2\text{S}_2\text{O}_3$  may be required giving a false higher value for arsenic.

TABLE I  
Analysis of carbarsone powder

Sample	Per cent ash (std.—not more than 0.1 per cent)	Per cent loss when heated (std.—not exceeding 1.1 per cent)	Melting point* (std.—169°C. to 171°C. with decomposition)	Per cent Arsenic (std.—28.1 to 28.8 per cent)	Per cent Nitrogen (std.—10.7 to 11.0 per cent)
Indian-made carbarsone powder no. 1	0.5	4.02	172°C.	27.78	10.8
" " " " 2	0.3	4.25	171°C.	27.53	10.8
" " " " 3	nil	0.6	173°C.	28.46	11.3
" " " " 4	0.09	1.73	172°C.	27.83	9.5
" " " " 5	nil	0.8	176°C.	28.22	11.0
American-made carbarsone powder 'Lilly'.	nil	0.9	177°C.	27.76	11.0
Powder obtained from capsule of 'Bangalore Brand' carbarsone.	..	..	178°C.	27.34	10.8
Powder obtained from capsules of 'Lilly Brand' carbarsone.	..	..	186°C.† (does not melt up to this temperature).	23.22 or 0.697 gm. as per capsule or 0.2424 gm. carbarsone.	

\*Uncorrected.

†Indicates that there is some other substance along with carbarsone powder in the capsules.

in capsules, and it was possible to examine these in strict conformity with the tests laid down. The findings are given in table I. Data obtained from American-made carbarsone powder and capsules are given side by side.

It will be seen from the table that, excepting no. 4, all the four samples agree very closely in their arsenic and nitrogen contents with the N.N.R. figures or the figures obtained for 'Lilly Brand' carbarsone powder. The percentages of ash and of 'loss on heating' of samples nos. 1 and 2 are higher, indicating the existence of moisture and traces of inorganic impurities in these samples. In sample no. 4, the arsenic content is distinctly lower, and the nitrogen content is also slightly below the minimum N.N.R. figure. Presumably there is some defect in the final stages of purification of the compound in this instance. This presumption gains support from the fact that sample no. 4 was found to contain a lower percentage of arsenic and nitrogen when it was first submitted for test in the laboratory. The same company submitted sample no. 5 later after further purification, which agreed in almost all respects with the theoretical standards.

The difference observed in the melting points, which are usually sharp, is significant. In three samples including that of 'Lilly' carbarsone, the melting point is higher than the specified limit of 171°C. In only one case (no. 2) the figure agreed with the upper limit. This may be due to the amount of moisture present tending to depress the melting point.

#### *Carbarsone tablets*

Most of the local brands of carbarsone are put up in tablet form, as capsules are not available in sufficient quantities in India. These tablets are being used in large quantities in the Army, and there is no evidence yet to indicate that these are in any way inferior in clinical value to the carbarsone capsules. Lilly and Company have also adopted the tablet form in some of their recent packings.

More than 100 batches of carbarsone tablets have been analysed. Table II gives the arsenic and carbarsone (calculated from arsenic) contents of nearly 50 representative samples. The analytical data on carbarsone tablets (Lilly brand) are also included for purposes of comparison. It is seen from an analysis of the data that the average weight of the tablets is 0.3349 gm. in which the average arsenic content is about 0.0646 gm. with a carbarsone content of 0.226 gm. This is lower than the claim usually made for each tablet to be 0.25 gm. However, as this finding agrees in general with the carbarsone content of American-made tablets, this may be considered as acceptable for all practical purposes. It is probable that full recovery of arsenic from tablets is not possible with the method employed by us for its estimation, or the carbarsone content varies

slightly on account of variations in the weight of individual tablets, which is inevitable in the process of tabletting.

TABLE II  
*Carbarsone tablets\**

Number	Weight of a tablet in gramme (average of 10 tablets)	Quantity of arsenic per tablet	Calculated quantity of carbarsone per tablet in gramme
1	0.3376	0.0664	0.227
2	0.3161	0.0681	0.230
3	0.3209	0.0674	0.227
4	0.3209	0.0671	0.227
5	0.3192	0.0700	0.236
6	0.3197	0.0685	0.231
7	0.3432	0.0728	0.252
8	0.3432	0.0728	0.252
9	0.3433	0.0686	0.237
10	0.3432	0.0670	0.232
11	0.3457	0.0698	0.242
12	0.3462	0.0687	0.238
13	0.3482	0.0656	0.227
14	0.2551	0.0565	0.195
15	0.3060	0.0633	0.219
16	0.3276	0.0569	0.197
17	0.3270	0.0613	0.212
18	0.3180	0.0703	0.244
19	0.3180	0.0732	0.257
20	0.3098	0.0548	0.190
21	0.3497	0.0630	0.218
22	0.3287	0.0613	0.212
23	0.3573	0.0735	0.255
24	0.3500	0.0654	0.226
25	0.3805	0.0663	0.230
26	0.3478	0.0634	0.220
27	0.3486	0.0663	0.229
28	0.3428	0.0623	0.216
29	0.3659	0.0686	0.238
30	0.3483	0.0649	0.224
31	0.3771	0.0712	0.248
32	0.3621	0.0634	0.220
33	0.3119	0.0614	0.213
34	0.3327	0.0626	0.217
35	0.3492†	0.0649	0.225
36	0.3331	0.0605	0.210
37	0.3298	0.0617	0.214
38	0.3624	0.0626	0.217
39	0.3554	0.0634	0.220
40	0.3732	0.0648	0.225
41	0.3073	0.0712	0.247
42	0.3053	0.0706	0.245
43	0.3279	0.0630	0.219
44	0.3339	0.0645	0.223
45	0.3178	0.0600	0.208
46	0.3262†	0.0640	0.222
47	0.3254†	0.0663	0.229
48	0.3294†	0.0639	0.221

\* Analysis for arsenic was carried out in every case by grinding the tablets to a fine powder before

† by Lilly & Co.

*B. Clinical trials.*—Chronic amœbiasis is one of those diseases which offer considerable difficulties in treatment to the physician practising in the tropics. The permanent eradication of the firmly established and chronic relapsing infection, with the mucous membrane of colon more or less extensively involved, is

unachievable in a short time by drug therapy alone. The evaluation of the efficacy in such a condition of a particular remedy is therefore not an easy matter. Neither the failure to ameliorate symptoms of the disease in any one case nor the temporary improvement of the diarrhoeic condition with disappearance of the parasites in one or two stool examinations are safe criteria for judgment. At least six or more negative examinations of stools on different days after cessation of a full course of treatment should be considered as the index of a 'cure', on which some reliance can be placed, and on which opinion as to prognosis of a case can be given.

In the clinical trials with Indian-made carbarsone, every effort was made to assess the value of each brand under carefully controlled conditions in the Carmichael Hospital for Tropical Diseases. A sufficient number of cases have not been treated to enable the authors to give a comprehensive opinion on all brands, but the general impression has been favourable, and no significant and noticeable differences were recorded, which could be accounted for by the differences in the response of one brand over another brand of carbarsone. General satisfactory results, as evident by improvement in appetite, a feeling of general well-being and gain in strength and body-weight, were also recorded in the treatment of many ambulatory cases, though it is realized that the evidence of a temporary relief of symptoms in such cases may not be taken as a true index of cure.

Chopra, Sen and Sen (1935) carried out comprehensive trials with one brand of carbarsone (Amibiarson—B. C. P. W. & Co.) and found a satisfactory cure rate (ratio of probable cures to failures = 5 : 1) as compared to carbarsone, Lilly (ratio of probable cure to failure = 5.75 : 1). Recently, Gupta and Chatterjee (unpublished) have completed another series of tests with an Indian-brand of carbarsone with equally encouraging results.

#### Comments

Judging from the evidence at hand (data of chemical analyses and clinical trials), the opinion may be expressed that Indian-made carbarsone is a satisfactory equivalent of the imported product. All the brands examined do not approach the theoretical degree of purity, but this difference is of a minor degree, and apparently does not affect the anti-amœbicidal efficacy of the drug to a measurable extent. Perhaps the same degree of purity needed in a drug intended for parenteral therapy is not necessary for a drug to be used by the oral route. However, some of the manufacturers would do well in insisting on a higher degree of purity up to theoretical standard, which should not be difficult to attain, if elaborate attention is paid and more stringent checking and control of the finished product is made before releasing the

substance into the market. From the large number of trials given in human patients, it appears probable that little, if any, untoward reactions would be encountered if any of these brands are administered in therapeutic doses indicated for carbarsone (Lilly). A reasonable assumption may also be made that the clinical results would be comparable with the imported brand of carbarsone.

While it is a matter of satisfaction for workers in the field of drug research and standardization to know that Indian-made carbarsone is of acceptable quality, it must not be forgotten that for some of the raw materials needed in the synthesis of this compound, India is dependent on foreign sources. Carbarsone,  $\text{CO}[(\text{NHC}_6\text{H}_4\text{AsO}(\text{OH})_2)_2]$ , is generally prepared by shaking a well-cooled 10 per cent aqueous solution of atoxyl with the calculated amount of carbonyl chloride dissolved in toluene (20 per cent). The resulting paste is washed successively in water and alcohol and the residual carbamide is dissolved in aqueous sodium carbonate and precipitated by hydrochloric acid (Morgan, 1918). Atoxyl is understood to be produced in small quantities in India from basic ingredients available in the country but some of the other items must still be imported. The supply of carbarsone of Indian manufacture would therefore be always limited in relation to the demand of the country where amœbic infection is fairly frequent.

#### Summary

Barring certain minor differences in chemical characteristics, Indian-made carbarsone is a satisfactory equivalent of imported carbarsone, and may be safely used wherever the latter is indicated.

#### Acknowledgment

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## 'LIPOID NEPHROSIS' CURED AFTER AN ATTACK OF TYPHOID FEVER

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SEVERAL observers have previously noticed that intercurrent febrile diseases may bring about an improvement and amelioration of symptoms in 'lipoid nephrosis'. The most common febrile disorders influencing the condition mentioned are various types of pneumonia, bronchitis, rhino-pharyngitis, erysipelas, otomastoiditis, sinusitis, etc. Rapid subsidence of massive oedema in terminal infection of nephrosis is also not an uncommon feature. Amongst the cases reported, that of Karaesony (1925) is worth quoting: 'general anasarca disappearing on two occasions immediately after the crisis of lobar pneumonia when all other available measures failed previously to reduce the tissue fluids'. Aldrich (1926) also reported three cases which were cured apparently after severe streptococcal infections.

The case under review merits recognition as it furnishes an additional evidence that a case of lipoid nephrosis may be apparently cured by a febrile disease, viz, typhoid infection. The following is the summary of the case notes:—

Male child, aged 4, with a history of steadily increasing puffiness of the eyelids, more prominent in the morning. Urine showing the presence of fair quantities of albumin and sediment containing hyaline casts. In spite of the treatment for albuminuria the oedema, shifting with position, spread gradually and progressively. Ascites was noticed to develop later on. Urine examination at this stage revealed the presence of albumin 1.5 per cent in Esbach's albuminometer. Specific gravity very high and the chloride output negligible. Centrifuged deposits containing casts mostly hyaline and few granular. The blood chemistry: serum protein below 4 gm. per cent in three analyses out of four and serum albumin below 1.8 gm. per cent in two analyses out of four. Blood calcium 7.5 mgm. and blood cholesterol 350 mgm. per 100 c.cm., but there was no abnormality in non-protein and urea nitrogen.

The patient responded with variable results to parenteral administration of hypertonic glucose solution along with 10 per cent calcium gluconate. Known diuretics made very little impression on the oedema. He was kept on salt free and high protein diet. After an illness of about 12 to 14 months, the child got an attack of fever of continued type which eventually proved to be of the enteric group. The blood examination was done on the 11th day of the fever and gave a positive Widal reaction against *B. typhosus* in 1 in 250 dilution. The boy developed diarrhoea at the end of the first week of the fever, and so was put on sulphaguanidine treatment which not only helped to clear up the diarrhoea but the height of temperature also diminished and the patient became fever-free after 21 days. Urine examination, early in the second week of the course, showed the presence of albumin and hyaline and granular casts, and oedema practically cleared up at this stage. During convalescence from this fever with the complete disappearance of the oedema, albuminuria cleared up, and after 6 months his serum protein returned to almost normal figures, general health improved, and to all intent and purposes he was cured of nephrosis.

The main features of the case are massive oedema, marked albuminuria, hypoproteinaemia

and hypercholestraemia. The absence of red blood cells in sediments of the urine, and the normal renal function with no change in non-protein and urea nitrogen, differentiate the case from one of glomerulo-nephritis. The complete disappearance of the albumin from the urine and subsidence of massive oedema after an attack of fever (enteric) is another proof of the case being uncomplicated 'lipoid nephrosis'.

The mechanism of oedema formation in true lipoid nephrosis can be best explained according to Sterling's views on fluid exchange in the body. As a result of albuminuria the plasma proteins are reduced to a considerable extent. The colloid osmotic pressure of the plasma is no longer sufficient to counter-balance the hydrostatic pressure in the capillaries, and hence fluid is forced out of the blood into the tissue spaces. In this particular case, during the course of the fever (specially in the second week) certain changes must have taken place to alter this condition; instead of more fluid being pushed into the tissues, the tissue fluid was dragged back by the osmotic effect of the non-diffusible plasma proteins, which is only possible when the plasma proteins are increased. Epstein (1928) considered the decrease in oedema after infection in lipoid nephrosis to be due to increased protein metabolism. An increased disintegration of proteins in the blood by fever is a secondary factor. It has been observed also that polypeptides in the blood in typhoid cases increase during the first week and reach their maximum in the second week. This increase persists for some time as also does the increase in the index of cleavage of polypeptides. These changes seen in typhoid, or similar changes produced in other ways, e.g., increased protein metabolism or non-specific protein shock, may be responsible for altering the low colloid osmotic pressure of the plasma, with marked diuresis and the subsidence of the massive oedema, but how they bring about a cure of the condition is very difficult to explain.

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## A Mirror of Hospital Practice

### TRAUMATIC CEREBRAL HERNIA

By B. HALDER, M.B.

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CEREBRAL HERNIA, though very rarely met with in civil practice, is almost always a sequel to serious head injury. A compound fracture of the skull, a tear of the membranous coverings of the brain and an increase of intracranial pressure are the three important causes that are usually responsible for the pathological condition. An injury which gives rise to a localized



weakness of the osseofibrous coverings of the brain matter leads to the development of such a complication. Such injuries lead to a free drainage of blood and, due to the natural decompression caused by the opening in the skull bone, the symptoms are less severe than the injuries would lead one to expect. In fact, grave and alarming symptoms and sequelæ are more often seen in closed head injuries than in open ones.

*Case report.*—S., a Mohammedan male, aged about six years, was brought to the hospital on 2nd July, 1943, in an unconscious state, having been knocked down by a running train. Examination revealed an injury to the vault of the skull on the frontal and parietal regions of the left side. On cleaning, the wound showed pieces of diploë, some lying loose but a few attached to the tissues. The wound was about 7 inches long and had a Y-shaped end on the left frontal angle, where examination revealed a portion of brain matter extruded and lacerated; a quantity of cerebrospinal fluid was detected in and around the wound; in this area a big piece of skull bone was missing.

The whole wound was cleaned and stitched after apposing the scalp margins and putting some sulphonamide powder into the wound, but difficulty was experienced at the junction of the limbs of the Y-shaped wound as the margins of the scalp could not be apposed even after scraping away a portion of the cerebral substance that had already been expelled out of the skull cavity and was lying on the anterior part of the wound. On the second day the child was brought with retention of urine and fæces which was relieved by an enema. The wound was not opened but the superficial dressings only were changed as they were soaked with blood and cerebrospinal fluid. The patient was comatose—no temperature.

Gradually the general condition of the child improved, and he began to respond to questions quite normally.

On the eighth day the wound was opened and the stitches were removed. All the stitches took perfectly, leaving a raw area on the front part where the brain was exposed, and from where cerebrospinal fluid was still oozing and soaking the dressings daily.

As days passed, this part began to swell up gradually till the whole swelling came up to the size of a ping-pong ball, and this tumour was diagnosed to be one of cerebral hernia. Visible pulsation was noticed, and cerebrospinal fluid was still oozing freely from the lower part of the tumour. Within a few days the child had a high temperature which lasted for four days, and M&B 693 was freely administered as the fever was thought to be due to infection of the cerebrospinal fluid. The fever was checked, and the tumour was dressed every day with acriflavine lotion. The illustration shows the size of the tumour about one month after the accident (see plate X).

In accordance with the usual textbook treatment, the application of formalin soaked in a piece of gauze was started, with occasional dressings of absolute alcohol, as the child was developing conjunctivitis due to daily applications of formalin (the tumour being close to the left eye and the vapour of formalin irritating the eye). After a few days' application, a hard black crust began to form on the wound, and the cerebrospinal fluid leakage began to get less and less till it stopped. An ulcer also gradually began to form at the base of the tumour, on a level with the adjacent scar tissue, which gradually began to cut the tumour off the scalp till eventually in a month's time the whole tumour, which looked like a thick scab, separated from the scalp leaving a small ulcer. It took another fortnight for the ulcer to heal completely and for the skin to grow over it. A distinct gap with sharp margins can now be felt in the skull at the site of the scar. This part of the scalp is very thin and soft, and throbbing, though less prominent than before, is visible at that area. No deficiency in the mental outlook is noticed, and no neurological symptom is complained of by the patient.

Points to note :—

1. Such a serious injury with laceration and expression of the brain substance does not necessarily mean death or serious neurological deficiency symptoms as is commonly supposed.

2. Cerebral hernia developed at the site of the deficiency in the skull bone where the meninges were also torn.

3. Infection of the cerebrospinal fluid is a complication which was efficiently checked by the prompt administration of sulphapyridine (M&B 693).

4. Spontaneous cure of the hernia with mediæal applications occurred without thorough plastic operation and the attendant complication and difficulties.

5. The case was treated in the out-patient department throughout.

6. Injury to the left frontal lobe of the brain does not lead to appreciable motor or sensory loss or late neurological sequelæ. Memory and intellect are apt to be affected as a late, after-effect.

## A CASE OF VOLVULUS OF THE SIGMOID COLON WITH AN UNUSUAL POST-OPERATIVE COURSE

By JAGDISH SINGH, F.R.C.S.E., F.R.C.S. (Eng.),  
D.L.O. (Lond.)

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A HINDU male, 48 years old, was referred to the surgical out-patient department on account of absolute constipation and vomiting for eight days.

On clinical examination, the patient was found to be a thin man with a long-standing history of



constipation. There was colicky pain in the abdomen which was distended, especially in the flanks. The tongue was rather dry; rectal examination did not reveal any cause of obstruction. The pulse was 120 per minute, temperature in the mouth 98°F., blood pressure was 120 mm. Hg. systolic and 80 mm. Hg. diastolic. The urine contained traces of albumin; the vomit was bile coloured. The patient was recommended for admission but he refused and went home. He was brought back at 9 p.m. in the same condition. A high enema was given but there was no passage of flatus or faeces. During the eight days of his present sickness, several doses of castor oil and two or three enemas had been administered without producing any relief. A diagnosis of volvulus of the sigmoid or growth of the left half of the colon was made, and laparotomy was advised. The patient agreed to submit to operation as he had tried everything else.

The laparotomy was performed under spinal analgesia (1½ grains of procain in 2 c.cm. of distilled water) and with a median sub-umbilical incision. As soon as the peritoneum was opened, much blood-stained fluid escaped, and it was found that sigmoid flexure was twisted on itself through one complete turn. The twist was gently undone and examination showed the parts to be viable. Just after the twist was undone, the patient passed a very copious fluid motion on the table. A long rectal tube was passed to prevent the recurrence of the volvulus. He was given about 2,000 c.cm. of 5 per cent glucose in saline by the intravenous drip method during the 36 hours following the operation, and the post-operative course was quite smooth till the 10th day.

On the 10th day the patient drew attention by complaining that his dressings felt wet. On examination, it was found that the scar was open for ½ inch in its middle but the wound was not gaping. On the 12th day the patient complained that he vomited several times during the night and did not pass any flatus or faeces. Rectal examination revealed the presence of dry faecal matter in his rectum. A soap-water enema produced a fair result. Next day it was reported that his condition was worse; vomiting was more frequent, and there was absolute constipation. Rectal examination again revealed the presence of faeces. His tongue was quite dry, there was hiccough, and the quantity of urine passed in 24 hours was 3 ounces. An enema was administered with a fair result. He was given 700 c.cm. of isotonic sodium sulphate (4.2 per cent) by the intravenous drip method. The blood was examined for blood urea level, and it was found to be 72 mgm. per 100 c.cm. The condition of the patient improved markedly, and isotonic sodium sulphate solution was repeated once again after 12 hours. The improvement continued, and the patient was discharged, cured, on the 21st post-operative day. Since his discharge three months ago repeated

urine and blood urea examinations have shown normal results.

Points of interest are (1) eight days' history before treatment, (2) the absence of severe pain and distension, (3) the value of rectal examination to exclude recurrence, and (4) the value of intravenous sodium sulphate as a diuretic.

## TRANS-PLEURAL OESOPHAGOTOMY FOR A FOREIGN BODY

### A CASE REPORT

By MUKUNDRAY K. PARIKH, F.R.C.S. (Edg.)

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THE patient, aged 20, was admitted into the hospital on 2nd December, 1943, with a history of dysphagia for 15 months. To begin with, he could swallow semi-solids and fluids but later he could swallow fluids only, and at times even this was impossible. There was no history of syphilis, and physical examination revealed no obvious cause of the condition. X-ray examination after a barium swallow revealed complete blockage at the level of the 4th dorsal vertebra visible on screening; a radiogram revealed that the blockage was produced by a denture.

The patient now remembered that 15 months ago he had an accident while riding a horse, and that in this accident he lost his denture. He had been taken to another hospital where unsuccessful attempts were made to remove the obstruction by means of an oesophagoscope.

We decided on operative removal, and the pre-operative treatment consisted of intravenous saline and glucose. As nitrous oxide was not available a basal anaesthetic was given followed by chloroform. The patient was placed in the right lateral position but was kept sitting up. A J-shaped incision was made parallel to the vertebral border of the scapula starting from the 1st rib. The trapezius and the rhomboid muscles were incised and the 2nd, 3rd and 4th ribs were excised subperiosteally up to the end of the transverse processes of the vertebrae. The articular ends of the ribs were disarticulated; 2½ inches of each rib were removed. Since further space was needed the transverse process of the 2nd, 3rd and 4th dorsal vertebrae were also excised. The parietal pleura was incised, and the left lung collapsed but there was no respiratory distress. Exploration and palpation of the oesophagus to the left of the aorta revealed nothing, and while the finger was touching the structures below the arch of the aorta there was a very deep inspiratory movement and the pulse stopped temporarily.

A stomach tube was then passed to indicate the site of the obstruction but this did not clarify the situation. The collapsed lung was then drawn towards the mediastinum, and it was found that the lung was adherent to the oesophagus in one area; in fact there was a mediastinal abscess around the oesophagus up to this point. The lung was further separated, and the foreign body was localized as being at the site of the abscess. The oesophagus was then opened longitudinally to the left of the aorta and the denture was removed. There was marked dilatation of the oesophagus above the denture. The oesophagus was closed with sutures, the wound in the parietal pleura was closed, and the muscles, deep fascia and skin were sutured layer by layer. The patient was turned upon his back and gastrostomy was done.

The patient came round from the anaesthetic, was given plenty of glucose and saline and was kept under an oxygen tent. He was cheerful and talkative. Nine hours after the operation he collapsed suddenly and died within two minutes. The death was attributed to post-operative shock in a patient with inanition due to starvation.

# HIGHLY POTENT WHOLE LIVER EXTRACT

HG % RBC count

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90	4.5
80	4
70	3.5
60	
50	
40	
30	



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# Indian Medical Gazette

MAY

## 'SUBSTITUTES FOR QUININE' AND MEDICAL ADVERTISING

THE widespread advertisements in the lay press and even in the medical press in India of 'specifics' for malaria, 'rapidly effective in all forms of malaria', often 'containing no quinine or arsenic,' 'better than quinine or atabrin', cannot be too strongly condemned, and should deceive no medical man. Nevertheless, some are deceived and enquiries are sometimes made regarding these specifics. The editor has had to refuse many advertisements of this nature submitted for publication.

He has examined some of these advertised remedies. Most of them contain a little quinine, not enough to be of any real use in severe malaria; some of them contain some arsenic which has no action on *P. falciparum*; one has been an antimony preparation which when tested showed practically no action in malaria; still another contained sulphapyridine which has a slight action in malaria; some contain perhaps in addition to a trace of quinine, some Indian herbal remedy for fever; some contain only the amorphous alkaloids of cinchona which have a limited action in malaria.

Now some of these preparations (always made from cheap ingredients but put up under a fancy name and at a fancy price) have some slight action in malaria, and if they were advertised as having a mild action in malaria which might be of some value in the milder malaria in the absence of quinine or atabrin, and also if they were sold at a reasonable price, one might not be able to criticize strongly. At present they are advertised in such a way as to deceive the public and even the medical profession. The name of a medical man is often cited as having tried and proved the value of these products, or they are advertised as having been scientifically tested in the 'research laboratory' of the firm. It is very noticeable that few, if any, of these products are marketed by Indian chemical manufacturers of repute. They are mostly marketed by firms, by 'research laboratories' or 'research institutions' which have rapidly appeared and multiplied during the war, most if not all of which have no laboratory worth the name and no research facilities at all; most of them consist of small shops or godowns in a back street where quinine, atabrin and other remedies are bought from

the black market, and a very small amount of these drugs is made up, usually in the form of pills, with other material which has no anti-malarial action.

The sale of these products is widespread and constitutes a public danger. The anti-malarial action, if any, is completely inadequate to control a serious infection with *P. falciparum* which is a menace to life; it may exert a little control over mild *P. vivax* infections which are not a menace to life. As for preventing deaths from malaria, or being of any real value in the treatment of malaria in the general population, they are perfectly useless. Not only are they useless but they are a danger. A patient buys these preparations and takes them at his home, and delayed recovery or even death may occur; whereas if they were not available he would possibly go to a hospital or dispensary and might get proper treatment.

The whole question of medical advertising in the lay press in India is one which demands attention. One has only to pick up the daily papers and periodicals published in this country to see the evil. In addition to the many spurious cures for malaria, one sees advertised cures for leucoderma, leprosy, tuberculosis, hydrocele, filariasis and dozens of other complaints. One sees many advertisements of remedies for impotence and other sexual disorders; one also sees many advertisements for remedies for 'suppressed menses', the remedies being obviously abortifacients. One sees other advertisements inviting people to write an account of their symptoms and to send money in order to receive the prescribed remedies. One comes across patients who have spent all they have and gone into debt to buy proprietary remedies for incurable diseases. The whole business is a ramp and a rapidly growing one.

This problem is not confined to India. It has been seen and is still seen in other countries, perhaps in not quite so blatant form. It has been seen in the United States and in Great Britain where steps have been taken to control it. The most efficient method of controlling it is for newspapers and other publications to refuse to publish such advertisements. The following, extract from the *Journal of the American Medical Association* describes such a step voluntarily taken by the Newspaper Proprietors' Association in Great Britain:—

'Blatant claims to cure all sorts of diseases made in the newspaper advertisements of proprietary medicines have long been a scandal. At last, this practice is to be checked. The Newspaper Proprietors' Association has unanimously adopted the following rules: (1) No advertisement will be accepted for any medicine or treatment which is claimed to be effective in Bright's disease, cancer, tuberculosis, diabetes, epilepsy, fits, locomotor ataxia, disseminated sclerosis, osteoarthritis, spinal, cerebral and venereal diseases, lupus or paralysis, or for preventing any of these ailments; for the cure of amenorrhœa, hernia, blindness, rheumatoid arthritis or any ailment of the auditory system; for procuring miscarriage, for the treatment of habits associated with sexual indulgence, or for any ailment connected with these habits. (2) No advertisement will be accepted

from any advertiser who by printed matter, orally or in his advertisement, undertakes to diagnose any condition or to receive a statement of any person's symptoms with a view to advising or providing for treatment by correspondence. (3) No advertisement will be accepted containing a testimonial other than one limited to the actual views of the writer, or any testimonial given by a doctor other than a recognized British medical practitioner. (4) No advertisement will be accepted containing illustrations which are distorted or exaggerated to convey false impressions. (5) No advertisement will be accepted which may lead persons to believe that the medicine emanates from any hospital or official source, or is any other than a proprietary medicine advertised by the manufacturer for the purpose specified, unless the advertising agent submitting the copy declares that the authority of such hospital or official source has been duly obtained.

'These rules are now in operation in all the London morning, evening and Sunday newspapers. Also advertisements will be submitted to medical scrutiny and the products advertised to chemical analysis if this is considered necessary. This is the first time leading newspapers have unanimously laid down and insisted on a standard of control over claims made in advertisements'.

We would draw the attention of the All-India Newspaper Editors' Conference to this matter. A strong step in this direction made by the Indian press would be very welcome. It would raise the tone of the press, and it would make it more respected in other countries (one foreign subscriber known to the editor stopped subscribing to an Indian journal because he found it full of advertisements of the types mentioned).

Some of the better newspapers in India carry very few such advertisements and appear to be exercising some control. Other newspapers of good standing in other respects appear to exercise little or no control. In these days of paper rationing and shortage of newsprint, it is particularly objectionable to see so much space taken up by what the Americans call 'unethical advertising' of medicinal remedies, making claims which have no scientific basis.

J. L.

## Special Articles

### MEDICAL ASPECT OF CHEST INJURIES

By R. VISWANATHAN, B.A., M.D., M.R.C.P.,  
T.D.D. (Wales)

LIEUTENANT-COLONEL, I.A.M.C.

Four years ago a man was brought to the chest department of a hospital in a precarious condition, having spat out a pint of blood. By ordinary conservative treatment the bleeding was controlled. He was otherwise in excellent health. He went through the whole routine examination for chest disorders. It was on x-ray examination of the lungs that the blade of a knife about three inches long embedded in the parenchyma of the lung was observed. But for the foreign body, the lung looked perfectly

healthy. On further enquiry, it was revealed that he had received a wound in the back ten years ago when he was caught in the midst of a fighting mob. The wound seemed to have healed up uneventfully, and the man had completely forgotten about it, as he never suffered from any disability consequent to the incident. The foreign body revealed its presence after ten years only by the symptom of hæmoptysis. I am narrating this report as an introduction to show what chest wounds, particularly foreign bodies, may not do immediately but may do later. But I am not offering this as a justification for Sauerbruch's (1942) suggestion to let sleeping dogs lie without immediate interference.

Without going into details we may remind ourselves of the following anatomical facts regarding the chest:—

(1) That the apex of the lung extends about one and a half inches above the middle third of the clavicle and hence may be involved in a wound of the neck, producing all the complications of a chest wound such as emphysema, pneumothorax and hæmothorax. (2) That the lower border of the lungs lies about two fingers' breadth above the pleural reflection. (3) That the main fissure of each lung is represented by a line starting from the second dorsal spine and crossing the fifth rib in the mid-axillary line to end at the lower border of the lung opposite the sixth costochondral junction. (4) That the internal mammary artery lies external to the outer border of the sternum, a fact worth remembering when taking Tudor-Edwards' suggestion of puncturing in the second interspace in front for aspirating pneumothorax. (5) That the heart lies behind the third, fourth and fifth costal cartilages and that portion of the body of the sternum which corresponds to these.

A knowledge of the main physiological principles connected with respiration and circulation will be extremely helpful in the diagnosis and treatment of injuries involving intra-thoracic viscera.

(1) Though anatomically the chest is divided into two distinct compartments by the mediastinum, it has to be considered as one cavity for the purposes of chest dynamics, as fluctuations in pressure on one side will be freely communicated to the opposite side through the mobile mediastinum, especially in a normal individual. It is not so in such pathological conditions such as in chronic tuberculosis where the mediastinum gets fixed as a result of inflammation in many cases, facilitating thereby opening into one compartment without producing much change of pressure in the other compartment. The mobile mediastinum is the cause of the greatest danger in chest wounds with an open pneumothorax which produces mediastinal flapping resulting in respiratory and cardiac embarrassment.

(2) With every quiet respiration, the tidal air which is breathed in and out averages 400 c.c.m. only, while the vital capacity of a normal individual is on the average 3,800 c.c.m. and the total lung volume is 5,500 c.c.m. During severe exercise, pulmonary ventilation is increased four- or fivefold. The closer the breathing approaches the vital capacity, the greater is the subjective discomfort of dyspnoea experienced. When the vital capacity is lowered, as in pneumothorax, wherein one lung is put out of function completely and the other lung is also pressed upon, the point of dyspnoea is reached much more quickly. Hence it is necessary to avoid all active movements in chest injuries. This physiological principle would also be borne in mind when transport of chest casualties by air is contemplated.

(3) The intrapleural pressure is sub-atmospheric, oscillating between  $-5$  mm. Hg. during expiration and  $-10$  mm. Hg. during inspiration. This is owing to the elastic recoil of the lungs, which will collapse if the chest is opened, due to the entry of external air into the pleural cavity.

(4) With a hole made in the chest wall, when the chest expands during inspiration, air will enter by both available inlets, i.e. the glottis and the new opening. The elasticity of the lungs and frictional resistance in the air passages always impede the entry of air into the lungs. If the other opening is big enough, practically no air enters the lungs even when the breathing is maximal in depth, the result will be death from asphyxia. Graham and Bell (1918) have calculated that in a person who would increase his tidal air to the normal vital capacity, the largest size of opening in the chest compatible with life is 5 by 10 cm. If the vital capacity is smaller, a lower limit is set to the maximal size of the tolerated opening. Once I almost lost a patient when doing thoracoscopy and pneumolysis, the assistant inadvertently leaving the canula for the cautery open for some time, resulting in a rapid rush of the air into the already air-filled pleural cavity. When an open pneumothorax is converted into a closed one, immediate and striking relief is obtained. This is not due to absorption of air but to the air during inspiration entering the lung only. Asphyxia can occur only when the minimal air requirement cannot enter the lungs. I have introduced 1,200 c.cm. of air in about seven minutes into the pleural cavity for controlling hæmoptysis without producing any visible respiratory distress.

(5) Another physiological factor worth remembering is the nervous control of respiration. It has been found experimentally in some cases of closed pneumothorax that rapid shallow breathing is produced reflexly via the vagi and is abolished by bilateral vagotomy. In acute pulmonary collapse, a disordered vagal reflex may be an important factor in producing increased pulmonary ventilation.

(6) Capps, by experimenting on patients with pleural effusion, found that the visceral pleura is insensitive, that pressure on the parietal pleura gives rise to sharp pain located accurately over the site of irritation, and that irritation of the central portion of the diaphragmatic pleura sets up a sharp cutting pain in the neck in the skin distribution of the third and fourth cervical posterior roots, while the peripheral part of diaphragmatic pleura is represented by the lower thorax, lumbar region and abdomen for referred pain sensation.

### *Classification of chest injuries*

Injuries to the chest can be grouped together under three headings :—

1. Internal injuries, (2) external injuries and (3) combined injuries. Group one comprises :—

(a) Traumatic asphyxia, (b) massive collapse, (c) rupture of the lung producing pneumothorax, hæmothorax, hæmo-pneumothorax or mediastinal hernia, (d) rupture of the lung with rupture of the parietal pleura producing surgical emphysema or mediastinal emphysema.

The second group includes simple wounds of the soft tissues and wounds with rib fracture.

In the third group are : (a) wounds opening into the pleural cavity producing open pneumothorax, (b) penetrating wounds of the chest with injury to the lung or heart or both, (c) wounds with foreign bodies.

*Traumatic asphyxia* is purely a medical condition. It is caused by the patient being

crushed, and is characterized by suffusion with blood of the face, neck, head and eyes, the face and neck being puffy and swollen. Bleeding from the nose and pharynx, and unconsciousness may occur. The condition is caused by over-distension of the capillaries and veins due to the absence of functioning valves in the jugular, facial and the cranial veins.

Bombing and depth charges have produced the condition of blast lung. A considerable amount of experimental evidence has accumulated, during recent years, to put blast injuries in their correct perspective, and to explain their pathogenesis. At first it was thought that the positive or the negative wave in the upper air passage produced the lung damage. Zuckerman (1940), however, experimentally showed that the effects are produced by the compression wave on the chest wall. Hayward (1941) points out that an explosion produces momentarily an enormous increase in air pressure, and the energy liberated is dissipated as a compression wave followed by a suction wave and partly as an evanescent but powerful wind, which also blows in all directions. Williams (1942) in his Hunterian lecture states that when a pressure wave impinges on an object, the subsequent effects depend on the relative density of the object. When the density is great, the pressure is deflected. When it is small it is changed into a wave of kinetic energy causing disruption of the object impinged upon.

The patient with blast lung is very much shocked. Pain in the chest, slight or severe hæmoptysis and short cough accompanied by dyspnoea are the typical features of blast lung. Physical examination may show a few moist sounds and sometimes signs of patchy consolidation. Radiograph usually shows multiple small scattered shadows throughout the lungs. Since hæmorrhages are present in both lungs, these shadows are probably produced by multiple lobular atelectasis. The treatment can be summed up in one phrase : masterly inactivity, absolute rest, absolute quiet, and administration of oxygen.

*Active massive collapse* of the lung without pneumothorax or hæmorrhage might occur as a result of chest injury. In all probability it is due to disturbance of nervous stimuli. One lobe or one whole lung becomes partially or completely collapsed. When not associated with other injuries, the symptoms may be mild, or may be so severe as to cause sudden death. The onset is sudden with dyspnoea, tachipnea, cyanosis, tachycardia, prostration and pain. The facies expresses great anxiety, and yet the patient does not look really sick. The signs are those which indicate marked displacement of the heart and mediastinum towards the side of the lesion. The chest wall looks flat, the intercostal spaces narrowed, the movements diminished and breath sound diminished but bronchial in character if audible. This is a condition to be borne in mind to avoid faulty diagnosis of pneumothorax



on the wrong side. The prognosis is usually good, but bad if the condition persists and is complicated by pneumonia.

*Pneumothorax* resulting from chest injuries may be internal or external, depending on whether the air enters the pleural cavity from the lung or from outside through an opening in the chest wall. Internal pneumothorax may be produced by a crushing injury to the chest; by a small splinter passing through the chest wall and rupturing the lung and getting embedded in the parenchyma; or by laceration of the lung by a fractured rib. Air in such a case enters the pleural cavity from the lung, while the track of the missile in the chest wall gets closed by the movements and overlapping of the muscles. Signs and symptoms of pneumothorax are the same whether they are produced by injury or by pathological conditions of the lung.

Depending on the character of the opening in the lung, three types of pneumothorax are seen. In the first, the opening closes with the collapsing lung due to air entering the pleural cavity, and once the lung gets collapsed, no more air enters, and the opening may get permanently sealed. In the second type, a fistulous opening occurs which allows free passage of air between the pleural cavity and the lung. In the third, a valvular opening allows air to escape into the pleural cavity during each inspiration but does not allow air to get out. The first is the least dangerous, the urgent symptoms produced immediately after the accident subside very soon as the air in the pleural cavity gets absorbed rapidly. In the second type, the presence of a free opening equalizes the intrapleural and intrapulmonary pressure, and hence a tension pneumothorax is not produced. The third type, called the *ingravescent pneumothorax*, is the most dangerous, as the pressure inside the pleural cavity increases rapidly until the patient dies of the respiratory and cardiac embarrassment.

In over 50 cases of spontaneous pneumothorax which I have seen, I have not experienced any difficulty in diagnosis, as the signs and symptoms, especially soon after the occurrence, are quite characteristic. In cases of chest injury, however, the presence of other complications, such as extensive injury to chest wall, may cause difficulties in the proper eliciting of signs in some cases. Pain, dyspnoea and cyanosis are the common symptoms. All the classical physical signs described in textbooks can be elicited only when the air inside the pleural cavity is under tension, as will be the case soon after an injury. In artificial pneumothorax, for instance, as a positive pressure is not aimed at, the signs are not all the same. The patient with pneumothorax after an injury is found in evident respiratory distress. There is bulging and widening of the interspaces, raising of the shoulder, and diminution of movements on the side affected. Vocal fremitus and vocal

resonance are diminished or absent. In cases where there is an opening allowing air to get in at each inspiration, distant amphoric breathing can be heard sometimes simulating the sound of a whistle. The characteristic coin sound can be elicited only when the air inside the pleura is under tension. With a patent opening, a cracked pot sound on percussion may be elicited. Concomitant hæmorrhage will correspondingly alter the signs. As the hæmorrhage increases, there will be a rising level of dullness if the patient is percussed in the sitting posture. In cases of chest wound, one should not attempt to elicit succussion splash which is the characteristic sign of hydro- or hæmo-pneumothorax.

Emergency front-line treatment consists in putting in a needle in the second interspace in front, two inches beyond the sternum, and leaving it *in situ* while the patient is being transported. Under ordinary circumstances the first two types do not require aspiration of air, but in cases of war injury, one will have no time to make certain that it is not the third type requiring continuous removal of air. Hence in all cases of chest injury with pneumothorax, a stout serum needle should be stuck into the pleural cavity before the case is evacuated to base hospital. A small punched out piece of thick paper inserted loosely inside the nozzle end of the needle will act as a valve, while a piece of sterile gauze spread over the mouth of the needle and fixed to the chest wall by adhesive plaster will keep the needle in position and prevent the paper from being displaced. As a base hospital measure of treatment where a special thoracic team should be working, I venture to suggest that all these cases should be explored by thoracoscopy. In that way it is possible to avoid subjecting the patient to thoracotomy. In a case of tension pneumothorax produced inadvertently during pneumolysis, I was able to explore and close the opening in the lung by coagulation at a subsequent sitting.

*Hæmothorax*, besides producing all the general symptoms of hæmorrhage, causes symptoms of respiratory embarrassment due to the presence of rapidly increasing fluid inside the chest. Physical signs are the same as those of pleural effusion in pathological conditions. By way of treatment I suggest early aspiration and replacement with air which will enable subsequent thoracoscopy. Thoracoscopy will certainly enable one to find out if the bleeding is going on or not, and whether the bleeding is from the chest wall or from the lung; in suitable cases the bleeding point can be cauterized without thoracotomy. I was able to do this in two cases of bleeding which occurred some time after the cutting of adhesions. Failing this procedure, thoracotomy should be attempted. Gas replacement will also facilitate radiographic examination of the underlying lung, as the presence of fluid will cause a uniform opacity of that side of chest without delineation of lung structure.

*Surgical emphysema* after chest injuries is in most cases due to rupture of the lung with associated solution of continuity of the parietal pleura. Hence there will invariably be pneumothorax as well. If subcutaneous emphysema exists without pneumothorax, and if it extends to the neck, mediastinal emphysema should be suspected. Parietal surgical emphysema is not by itself a dangerous condition. But a mediastinal emphysema is of grave omen, as it rapidly produces dyspnoea and circulatory disturbances, and the patient dies quickly unless relief is given by free incisions over the neck to let out air. In this connection it should be remembered that emphysema and pneumothorax after a chest wound can be produced by gas producing organisms also.

The second group of chest wounds is purely the concern of the surgeon.

In the third group the most dangerous form of chest wound is an open pneumothorax. I have already discussed the physiological basis of this danger. The patient rapidly passes into a state of asphyxia when during inspiration all the air gets into the thorax through the open wound and none through the trachea into the lung. The danger is worse still with a sucking wound which leads rapidly on to a tension pneumothorax. Hence the necessity of closing the opening at the earliest possible opportunity. In fact, that must be the first aim of first-aid treatment.

### Diagnosis

An accurate diagnosis, even on the front line, of the character, extent, and complications of the chest wound is of the greatest importance. The R.M.O. should see if the wound is penetrating into the chest cavity, and should be able to find out if there is pneumothorax or hæmorrhage complicating the chest wound. I am of the opinion that it is not difficult to find out the presence of these complications by physical examination alone and by careful assessment of symptoms. I consider that that disturbance to the patient which physical examination will involve is not going to materially alter the already precarious condition of the patient provided gentle handling is done. On the other hand, an early correct diagnosis will be life-saving in many cases. Displacement of the mediastinum, which is the common and characteristic sign of both pneumothorax and hæmothorax, can be easily found out by finding the position of the apex beat. But it is quite possible in shocked patients that this is not palpable. In such cases one should never omit to palpate the position of the trachea which may be found displaced from its usual central position. X-ray as an aid to diagnosis is of very great importance. Shenton's method of localization of a foreign body is the easiest and simplest available. Tomography has also a place in a base hospital chest centre. A simple tomographic attachment

has been described by Viswanathan and Kesava-swamy (1940). It does not cost more than a rupee to make. I have found it eminently workable and useable.

Prognosis in chest wounds depends on the character and complications and also on how soon and how efficiently surgical intervention is obtained. Zenker (1942) points out the early dangers to be :—

1. A chest wound may be overlooked in a patient who is very shocked.
2. Increasing hæmothorax.
3. Widely open pneumothorax.
4. Tension pneumothorax.
5. Mediastinal emphysema.
6. Associated abdominal and thoracic injuries.
7. The late danger—sepsis.

Serious sequelæ of chest injuries, especially of penetrating wounds with foreign bodies occurring even after 10 or 15 years, are unfortunately not uncommon, resulting often from delay or too conservative a method of treatment, and sometimes occurring in spite of efficient and prompt surgical intervention. These are pain over the chest wall, excessive mobility of the chest wall due to decostaliation, preventable by the constant wearing of a pad, aneurism of the heart, hæmoptysis as in the case cited; abscess of the lung, bronchiectasis, chronic emphysema with or without broncho-pleural fistula. This long list of late disabilities which exhibit themselves after years of freedom from any symptoms; which carry with them a high mortality rate, and which present serious and difficult problems in treatment at this late date, should make us pause and consider the advisability of early radical treatment.

The outcome of a chest wound, therefore, depends entirely on early treatment. Linberg (1940) attributes the low mortality rate of 2 per cent from chest wounds in the present-day Russian Army as compared to 30 to 40 per cent mortality in the 1914–18 war, to correct initial treatment and better organization by the institution of special thoracic teams. The concentration of chest cases in special hospitals or wards is fundamental as they need the undivided attention of experts.

My thanks are due to D. M. S., India, for giving me permission to publish this paper.

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## THE GOAL BEFORE US, THE MAGNITUDE OF THE TASK AND THE PART IN IT OF THE MEDICAL WOMAN\*

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I TAKE it as a signal tribute to the great service of which I have the honour, for the time being, to be the head, that on the first occasion on which you have invited a member of the so-called stronger sex to preside on your Founder's Day it should be the Director-General, Indian Medical Service, on whom your choice has fallen, and on behalf of my service and myself I can assure you that this honour is greatly appreciated.

We are living through stirring times and the medical profession is, in keeping with its tradition, playing a full and not inconspicuous part in the great adventure in which the Allied Nations are engaged. It is indeed difficult to keep one's thoughts in any other channels than those which are connected with the prosecution of the war and the attainment of that complete and unconditional victory which, thank God, it is now possible to say is approaching the horizon, and of which, like that of the rising sun, the foreglow is now clearly discernible and is the object of countless longings and speculative glances. After night comes day; and after war comes peace which 'hath her victories no less renowned than war'. It is towards winning of these victories that the attention of thoughtful persons among the United Nations, from their leaders down to the sailors, soldiers and airmen in the ranks, is being directed in an ever-increasing degree; and never before has so large a proportion of humanity been so unanimously resolved that there shall be no return to the bad old pre-war systems, but that out of these years of struggle, effort and sacrifice shall emerge a better order of living for humanity as a whole and especially for the common man and the common woman.

This urge to develop is no news to you. The speeches of our leaders, the press and the radio have seen to that. Many of you will have been fortunate enough to have listened to the two recent broadcasts by Professor A. V. Hill, Secretary of the Royal Society, from Calcutta and from Delhi, and will have heard with enthusiastic approval his clarion call for Indian development. You will also have noted that in these broadcasts Professor Hill has placed the expansion of health in the very forefront of his programme.

It is for this reason that, when casting about for a subject on which to address you this afternoon, I found myself compelled to turn, however reluctantly, from my first choice—a

\* Being an address delivered at the Founder's Day celebrations of the Lady Hardinge Medical College, New Delhi, on 17th March, 1944.

subject which is very near my heart, *viz*, the Hippocratic ideal of professional ethics and practice. It was borne in on me that these are no times for philosophic reflections, however admirable; these are days in which each one of us must be up and doing something to preserve and to recreate a world in which there is room and leisure for philosophy.

It therefore seemed more appropriate for us to devote a few moments this afternoon to this post-war development which is so urgent and so much in the air, and especially to those aspects which concern health. With your permission, therefore, I wish to direct your attention to 'The goal before us, the magnitude of the task and the part in it of the medical woman'.

Throughout the civilized world there is now complete agreement that health is a basic human right. The human being is not consulted before entering this world, and should not, in equity, be exposed to preventable handicaps. It is therefore a primary duty of every sovereign state to ensure that its citizens have at their disposal all the necessary ingredients of positive health. What are these ingredients? They are:—

That there should be available:—

To every citizen:

- (1) ordinarily,
  - (a) an ample and pure water supply,
  - (b) foodstuffs of necessary purity,
  - (c) sanitary conservancy adapted to local needs,
  - (d) hygienic housing conditions, and
  - (e) adequate protection from preventable disease; and
- (2) when sick,
 

the necessary diagnostic, therapeutic and nursing care that his condition requires, should he desire to avail himself of it.

To every woman:

- (a) adequate care and advice when pregnant,
- (b) adequate obstetric assistance during labour with facilities for full institutional care (diagnostic, therapeutic and nursing) for such cases as require it, and
- (c) adequate qualified care of mother and infant during the lying-in period.

To every child:

- continuous medical observation (and, where necessary, treatment) during—
  - (a) infancy,
  - (b) toddlerhood, and
  - (c) school life.

To provide the India of the future with these ingredients is therefore our goal, and the task to which we should set ourselves.

As to the magnitude of the task, I propose to offer a few remarks:—

Positive health can only be secured in this world by constant, unremitting and co-ordinated human endeavour. The agents of this struggle

are doctors, nurses, health visitors, midwives, pharmacists and dentists, to mention only a few.

In designing a project, the experience of similar organizations elsewhere provide one, and probably the most reliable, index of its needs. It is not claimed that the figures I am about to quote, which are based upon Western countries, are an accurate estimate of India's needs, which can only finally be estimated by India herself in the light of experience. But they do form an indication of the size of the task and are intended as such and nothing more.

**Pharmacists.**—It is reckoned that for efficient health services 1 pharmacist for every 3 doctors is required. In the United Kingdom there is 1 to every 1,300 of population and in the U.S.A. 1 to every 1,100. In India there is 1 trained pharmacist to every 4,000,000 of population. 100,000 such pharmacists are required, and there are in India 75.

**Dentists.**—For every 3,000 of population there should be 1 qualified dental surgeon. In the United Kingdom the proportion is 1 to 2,700 and in U.S.A. 1 to 2,200. In India it is 1 to

#### THE MAGNITUDE OF THE TASK

##### *Requirements in personnel to bring India into line with modern trends*

Personnel	Available now	Proportion to population and to area		Required
Doctors .. ..	40,000	1 to 10,000 (U.K. 1 to 1,000).	1 to 40 sq. m.	300,000 on basis of 1 to 1,500.
Nurses .. ..	7,000	1 to 56,000 (U.K. 1 to 300).	1 to 226 sq. m.	778,000 on basis of 1 to 500.
Health visitors ..	1,000	1 to 350,000	1 to 1,582 sq. m.	70,000 on basis of 1 to 5,000.
Midwives .. ..	5,000	1 to 70,000	1 to 316 sq. m.	90,000 on basis of 1 to 4,000 (or per 100 births).
Qualified pharmacists	75	1 to 4,000,000 (U.K. 1 to 1,300 U.S.A. 1 to 1,100).	1 to 20,000 sq. m.	100,000 on basis of doctor to pharmacist—3 to 1 as in U.K.
Qualified dentists ..	1,000	1 to 350,000 (U.K. 1 to 2,700 U.S.A. 1 to 2,200).	1 to 1,582 sq. m.	120,000 on basis of 1 to 3,000.

The above figures are approximations and not exact estimates.

Let us now, subject to that proviso, first consider *doctors* :—

It is estimated that positive health cannot be assured to a nation unless and until they have a minimum of 1 doctor to every 1,500 of population. In the United Kingdom there is 1 doctor to every 1,000 of population. In India we have 1 to every 10,000. There are 40,000 medical practitioners registered in India to-day. To assure positive health to this sub-continent 300,000 are required.

**Nurses.**—Turning now to nurses, the minimum provision necessary to ensure positive health is 1 nurse to every 500 of population. In the United Kingdom there is 1 trained nurse to every 300 of population. In India we have 1 to every 56,000. There are 7,000 trained nurses registered in this country, and to ensure positive health to the people 778,000 trained nurses are needed.

**Health visitors.**—It is estimated that 1 health visitor is required for every 5,000 of population. In India to-day there is 1 health visitor to every 350,000. There are approximately 1,000 trained health visitors in the country, and 70,000 are required.

**Midwives.**—It is considered that to ensure positive health there should be 1 trained midwife per 4,000 of population, which works out at 1 trained midwife per 100 births. In India there is 1 trained midwife per 70,000 of population. There are approximately 5,000 trained midwives in the country, and 90,000 are required.

350,000. There are in the country approximately 1,000 qualified dental surgeons, and 120,000 are required.

This then is the task which lies before India in her post-war development in matters of health. It is only a part of the effort which she must make if she is to keep abreast of the progress and development of the world in general and the United Nations in particular. Lest it should be thought that the goal is Utopian and the task of achieving it in any measurable period of time impossible, it may be pointed out that a very similar measure of progress in health provision has, in fact, been achieved in Russia in the space of 20 years, starting from conditions which were in all essential similar to those obtaining in India to-day but without comparable advantages of communications such as this country possesses.

There are those who say that progress of this kind has only been possible by the practical application of the Marxian political philosophy. Such is not the case. Russia and the Marxian philosophy came to the parting of ways quite early in the execution of the industrial plans. The driving force behind the progress in Russia is not any political philosophy but the united and indomitable will of a whole people to place their country on the map of modern civilized progress.

It may also be argued that such progress could not have been achieved without drastic restrictions on the liberty of the subject. This

may, in part, be true; but I would remind my audience that the 'greatest good of the greatest number' is as much a democratic principle as is the 'liberty of the subject', and that what is required is not a clash between these two principles but their synthesis.

Other sceptics will say that the goal envisaged is admirable, but where is the money to come from? We have the authority of men like Professor Keynes and Professor Hill that money is 'the servant and not the master of policy'. Moreover, we have had for the past four years an irrefutable demonstration of this principle which has cost us dear in blood and sweat and toil and tears. Calculated in terms of money and in comparison with the wealth of the Western democracies, the resources of Germany were almost negligible, yet this has not prevented her placing in the field and maintaining for 4½ years the most highly organized, formidable and destructive fighting force the world has ever seen. If money had governed the prosecution of war, this conflict would have ceased long ago; but the driving force behind the prosecution of war is human energy and human productivity, of which money is only one convenient symbol. Exactly the same driving force has been behind the Russian progress in matters of health, and must be the motive power behind similar progress in this country and in the post-war world as a whole. Unless humanity devotes the same creative energy and ingenuity to problems of construction that it has hitherto shown in destructive activities, nothing lies before the human species but a gradual process of mutual and highly organized scientific destruction.

So far I have dealt with the goal before us and the task involved in its achievement. Let us now consider for a moment the share of the medical woman in that task.

Judging from the views I have heard expressed at interviews by young medical women who are candidates for admission to the various medical services, it is the ambition of the majority to devote themselves to the actual relief of disease among women and children. Such an ambition is natural enough, for there is, God knows, enough dumb misery and suffering among the women of India fully to occupy the energies and devotion of every medical woman in this country for many years to come. It is also an ambition with which I personally have very great sympathy, for gynaecology was my own first love; and in spite of the fact that force of circumstances had turned me into a 'Jack of all trades' with a bias to surgery, I justified the French proverb by as many and deliberate returns to gynaecology as circumstances permitted. Nevertheless, I venture to doubt whether this admirable and comprehensible ambition of the majority of women doctors is the only, or indeed the best, contribution that they can make to the task we have considered.

The scriptures tell us that 'There is more joy in heaven over one sinner that repenteth than over ninety and nine righteous persons that need no repentance'. The medical profession, I think, have this at least in common with the Saints in heaven that there is apt to be more satisfaction over one critical case, adequately treated, than over ninety and nine healthy human beings who stand in no need of treatment. While the attitude of the Saints in heaven towards the human soul may be, and probably is, morally excellent, I venture to suggest that the application of this outlook to the human body by our profession, though comprehensible, is medically very exceptionable. We have seen that positive health is only to be secured by constant, unremitting and co-ordinated human endeavour, and from this aspect the positive health of the ninety and nine should give us 99 times the satisfaction that we derive from the one successful case. At the risk of being platitudinous, I would remind you of the proverb that 'prevention is better than cure'. It is also very much cheaper.

A skilfully conducted abnormal labour which preserves both mother and child, or a difficult colpo-perineorrhaphy is a most satisfying achievement; but surely the decline in abnormal labours due to efficient ante-natal work and the decrease in repair operations due to the proper superintendence of labour and the puerperium is vastly more satisfactory from the point of view of the community, if less clinically interesting to the individual doctor.

One would therefore plead with both teachers and students to give to the preventive aspect of their work the predominant importance that is its due. This must be our constant pre-occupation if our goal is to be reached within any measurable period of time. It is, moreover, possible without the slightest diminution of that practical clinical sympathy and interest which is the distinguishing mark of our profession.

The field open to the medical women for service to the community in general and to women and children in particular, is both vast in scope and patetically inadequate in provision. Although when one looks back at the expansion which has taken place since the first medical women came to India from the United States in 1869, the retrospect is one of great and honourable achievement, medical women will be the first to concede that little more than the surface of the problem has been scratched. The following, among others, are the channels open to medical women in this country:—

(1) The all-India and provincial women's medical services.

(2) Appointments in hospitals, general and special.

(3) Private practice—urban and rural.

(4) The military medical services.

(5) Public health work and social medicine.

(6) Teaching institutions—medical education, both under-graduate and post-graduate.



(7) Industrial medicine—the care of the health of women in industry.

(8) Administrative posts.

(9) Medical research.

Let me direct your attention briefly to only some of them taken at random:—

*The field of public health.*—The fight against tuberculosis is as yet almost entirely in male hands, yet at least half the sufferers from this disease are women. Moreover, social customs which apply particularly to women form one of the most potent factors in the spread of infection. Tuberculosis, again, is a disease in which the success of preventive work far exceeds anything that has been found possible on the curative side. Improvement in housing conditions and the examination and protection of contacts have done more to diminish the mortality from tuberculosis than all the medical and surgical skill which has been directed to the treatment of the disease when contracted.

It has been estimated that there should be one tuberculosis clinic for every 50,000 of population, i.e., 8,000 tuberculosis clinics in this country. This postulates 8,000 medical women engaged predominantly on the prevention of this disease.

Half a million beds are required for the treatment of tuberculosis sufferers in India. Of this a quarter of a million will be women; and assuming that 1 medical woman can give efficient supervision to 100 patients, 2,500 medical women are required for the efficient treatment of the disease when contracted.

Tuberculosis work alone, therefore, calls for 10,500 medical women to be produced during the next, say, 50 years.

It is estimated that there are in India to-day two to two and a half million blind persons. It is not unreasonable to assume that half this number are women, and it is incontestably true that the majority of the conditions leading to blindness are contracted during childhood in the home. Yet the prevention and treatment of eye diseases in this country is, so far, almost entirely a male preserve. There is, therefore, a vast field open to the woman ophthalmologist.

Tuberculosis and blindness are both conditions which may be said to be contracted in the home. Moreover, it is the women and children who have to live in the home; yet how many housing improvement schemes have associated with them a medical woman?

*Industrial medicine.*—There is high authority for the belief that India stands on the threshold of a vast industrial expansion. Women are even now extensively employed in industry, and the scale of their employment must of necessity greatly increase in the near future, carrying with it the need for a large increase in the pitifully inadequate provision for industrial medicine generally and for the care of women in industry in particular.

*Social medicine* is a new name for an old need. In too many cases is the patient in

hospital regarded as a problem in symptoms and physical signs the solution of which involves the use of a drug or the knife, and a shorter or longer period of recovery; and the ultimate discharge from hospital is regarded as the end of that particular problem. Too often it is the end of only one instalment of a tragic serial. The true solution of the problem demands a knowledge of the environment from which the patient came and that to which he or she will return; and treatment can only be considered adequate when, in addition to the control of the immediate clinical condition, environmental circumstances which tend towards its repetition, or substitution by another clinical problem, have been similarly controlled. It may be said that this is the work of the Almoner. It is true that it constitutes the life work of that important part of any medical institution; but it is predominantly the care and responsibility of the medical man or woman in charge of the individual case. Realization of this fact has led to the establishment of a chair of social medicine at Oxford University, the occupant of which is no less a personage than the late Regius Professor of Medicine at Cambridge. Realization is also likely to be reflected in the training of the medical student who will be connected not only with the care of his patient while in hospital, but with the follow-up, in company with the Almoner, of the patient's progress after discharge. For many years to come, in the north of India at any rate, social medicine as applied to women and children, must inevitably fall into the sphere of medical women.

The need for great development in India of medical research and especially of clinical research is generally admitted. Not only in the special sphere of women and children, but throughout the vast research field golden opportunities of making real contributions to medical knowledge await the medical women: nutrition, hæmatology, immunology, malaria, filariasis are only some of the aspects holding special interest for workers among women, while the subject of pædiatrics abounds in unsolved problems of the child.

The primary and most clamant need of the future is more teachers. Teachers to train clinicians, public health workers and research workers. Teachers who, themselves eminent scientists and practitioners, shall be in whole-time and adequately remunerated employment, so that they may be free to give their entire attention to the teaching of the subjects entrusted to them, untrammelled by the necessity of extra financial provision for their present and future. Perhaps it is not Utopian to look forward to the establishment in this capital city of India, perhaps in this institution itself, of an 'Indian Johns Hopkins' designed primarily for the training of the teachers and research workers of the future, and accepting as candidates for entry only the cream of graduates in other



sciences. If some such project could be achieved, the enormous task of providing India with the instructors necessary to turn out the doctors of the future in the quantities needed, while it could not be called fulfilled, could at least be faced without despair.

Ladies and gentlemen, I have detained you too long with my reflections. I can only plead in excuse that they are very near my heart, and that once a man is mounted upon his hobby-horse he takes a lot of unseating. Nevertheless if any words of mine this afternoon have proved of interest or value to anyone of my listeners I am amply rewarded. I am absolutely convinced that we are on the threshold in this country of a vast and intense revival or, better, new birth of health activities, and I find it very much in my heart to wish that it were possible for me to start all over again and take some part in this renaissance. But the time is near when my generation of doctors must prepare for their exit from the professional stage, and when the torch which we have endeavoured to tend and to keep alight must pass into younger and more capable hands. In this hall are many such hands eagerly waiting to grasp the torch and to play their part in the Crusade. It is not the least of my privileges to-day to welcome these young and promising recruits, to bid them be of good cheer, for the fight, if long and tough, is intensely interesting, and to wish them God speed in the campaign against human suffering and misery—surely the noblest field open to human endeavour.

## Medical News

### A RED CROSS PUBLICATION

THE League of Red Cross Societies, Geneva, has started publishing a new periodical 'Hygiene—Medicine—Biology: Notes and Abstracts', the aim being to keep the national Red Cross Societies informed of scientific progress in these subjects, no doubt a difficult task in these days. We have received a copy of its first issue (July 1943) which contains summaries of important papers published in medical literature or of documents in the possession of the League Secretariat. It hopes to publish the periodical quarterly, and at present these 'notes and abstracts' are being distributed only to the Red Cross Societies.

### A MEDICAL SCIENCE EXHIBITION

A MEDICAL Science Exhibition was recently held at the King George's Medical College, Lucknow, under the auspices of the Clinical Society.

The Exhibition was divided under the following sections:—

(1) History of Medical Sciences—included an account of the Founders of Present-day Medicine and Surgery; their progress through ages, and a series showing stages in evolution of microscope, x-ray, glasses and blood transfusion, etc.

(2) Anatomy—(a) the unborn, (b) architecture (skeleton bones, etc.), (c) the internal machinery, (d) the plan of unity (comparative anatomy), (e) a

journey through ages (the story of the races that ruled the earth thousands of years ago).

(3) Physiology—(a) the blood, its composition and circulation, (b) what happens to the food you take? the dictators of digestion and what they dictate, (c) the special senses—showing how one sees, hears, speaks, tastes and touches, (d) how the muscles work? (e) urine—the abnormal constituents and what they indicate.

(4) Surgery—was illustrated with exhibits showing the diseases of various parts, artificial compliances and interesting surgical instruments.

(5) Ophthalmology—structure of the eye and its defects were illustrated by charts and specimens.

(6) Obstetrics and gynaecology—included specimens of various monsters and abnormalities of foetus.

(7) Medical jurisprudence.

(8) Hygiene—(a) peep in the inside of man, (b) his food, (c) his environment, (d) common diseases and their prevention, (e) personal and mental hygiene, (f) maternity and child welfare.

(9) Social diseases—displayed the world's greatest public enemies nos. 1 and 2 and the lesions caused by them.

(10) Pharmacology—(a) experimental section, (b) drug section, (c) endocrinology section.

(11) Pathology—(a) what diseases we get by microbes, (b) parasites and their harmful activities, (c) alcohol—its effect on internal organs, (d) something about tumours, (e) diseases our parents give us, (f) freaks of nature.

## Current Topics

### Warning on Use of Warmth for Treatment of Shock

(From the *Journal of the American Medical Association*, Vol. CXXII, 22nd May, 1943, p. 246)

IN the *Army Medical Bulletin* the warning is given that the enthusiastic application of heat for shock has inherent risks. The blood volume nearly always diminishes after severe injuries, because fluid has left the vessels either by haemorrhage or by oozing into damaged tissues or both. The consequent fall in blood pressure brings into play a vasoconstrictor mechanism which raises pressure by reducing the capacity of the vascular bed. It is not yet certain which parts of the vascular system are affected by this vasoconstriction, but undoubtedly the cutaneous circulation is much diminished and its capacity is considerable. Even in a normal person warming may increase the blood content of the skin by as much as a pint. When the superficial vessels are already constricted, far more than a pint may be brought to the surface and diverted from vital functions. Hence excessive warming may interfere with the body's endeavour to restrict its total vascular capacity and make a little go a long way. It may also accelerate loss of fluid from the surface by evaporation and sweating; it may accelerate metabolism of skin and muscle and thus jeopardize structures whose blood supply is impaired by local injury; and it may promote autolysis of damaged tissues and absorption of autolytic products. Experimentally it has been shown that general and vigorous heating of injured animals decreases their chance of recovery and hastens their end. The application of cold, on the other hand, though it lengthens their period of survival, does not increase their chance of recovery. Thus theory and experiment agree that casualties should be warmed in a conservative manner with blankets and hot water bottles applied after removal of wet clothes. More potent means of heating, such as a heat cradle, may be used when blood volume is being, or has been, restored by transfusion. But the heat should never be so great as to cause sweating, and limbs with

injured blood vessels or gangrene should not be warmed at all. As far as the 'cold' of shocked patients is compensatory, it is a symptom that should not be treated energetically unless its cause—reduction of blood volume—can be treated at the same time. Whereas warming plus transfusion gives excellent and prompt results, warming alone may be carried too far and lead to vasodilatation, circulatory collapse and death.

### Vital Statistics of 1942

(From the *Medical Officer*, Vol. LXX, 10th July, 1943, p. 9)

It is not often that a vital statistician, in discussing the statistics for a single year, gets the opportunity to give evidence of some truth which was previously only suspected. His success usually depends on his foresight and on the ability which he applies to the search. In discussing the vital statistics of 1942 Dr. Percy Stocks has uncovered one of these interesting observations which would have remained hidden had it not been for his experience in revealing the inner meaning of the data. Dr. Stocks shows that the death rate for civilian females in 1942—6.80 per 1,000 living—was 9 per cent better than the rate for any previous year. The corresponding rate for males was also below the previous record, but the fall was not so great as in the females. Such a decrease would be remarkable at any time, but in the third year of a total war it is so unexpected that search has to be made for some definite cause. Further analysis showed that the improvement in the death rates had commenced for certain ages in the year 1939. For both civilian males and civilian females the death rate at all ages under 45 showed a considerable decrease as compared with the rates for corresponding ages for the year 1938. It should be noted that the effect of recruitment at these ages is to exert a selective influence on the death rates, since the remaining civilian population consists of those who are most liable to succumb to the attacks of disease. The death rates at ages above 45 were for civilian males and females higher than the 1938 rates. When these data are compared with the corresponding figures for 1942 it is shown that the improvement had spread to all ages above 45. These findings suggest that some factor operated upon younger persons about the year 1939 and later on older persons also.

Dr. Stocks considers that natural or social causes could not have been responsible for this effect. On the other hand sulphonamide therapy was applied about the year 1939 mainly to younger persons, and later it was administered to persons of all ages. It is shown that at ages 1-5 there was in 1939 a remarkable fall in the death rates from diseases such as measles, pneumonia, cerebrospinal fever and illnesses in which death is liable to result mainly consequent upon streptococcal complications. This conclusion applies even when allowance is made for the natural variability of certain of these diseases. Dr. Stocks therefore concludes that the lives saved by sulphonamides in 1942 exceeded 100,000. This decrease was sufficient to neutralize the increase in deaths since 1938 attributable to the rising population of old people in the community.

Other diseases not usually influenced by sulphonamides produced death rates which were not so satisfactory. Especial interest is attached to the findings in tuberculosis. The deaths from respiratory tuberculosis at all ages had increased markedly in the war years, but in 1942 they fell to slightly less than the 1938 figures. The total deaths from all forms of tuberculosis were 11 per cent fewer than in 1941, and almost the same as in 1938 and 1939. The deaths from recent or unspecified syphilis numbered 893 in 1942 compared with 1,000 in 1938 and 963 in 1939. As syphilis kills late there will probably not be until after a considerable period any indication in the mortality rates of the present increase in primary syphilis. The rates for deaths from peptic ulcers

return to about the level of 1938. Deaths from diabetes had increased in 1939 and 1940, but since then there has been a decline. Dr. Stocks shows that this decline began after sugar rationing had been in force for a year.

Deaths from degenerative heart conditions and nephritis did not generally show any marked increase over the 1938 figures, though the 1939 rates had been somewhat higher than those for the previous year. On the other hand, it should be mentioned that the number of deaths from coronary diseases and from angina pectoris increased in 1942. This is an inevitable result of the aging of the population. This change in the age constitution of the population is probably also responsible for the increase of deaths from cancer which was noted in 1942. This year was also marked by a continuation of the decline in the deaths from three widely different diseases—rheumatism, exophthalmic goitre and diphtheria. When we consider that on *a priori* grounds an increase in deaths from rheumatism would have been expected in war time, it will be realized how little we know about these rheumatic conditions. On the other hand the deaths from diphtheria were 14 per cent better than the previous lowest figure, a decline of such an order as to suggest that something more than chance was operative. This decline should encourage everyone who believes that this disease can be successfully attacked long before the patient ever has much chance of being subjected to continuous heavy infection.

### Theophylline for Asthma

(From the *British Medical Journal*, Vol. I, 12th June, 1943, p. 731)

THE chronic asthmatic has to be his own doctor, at least to the extent of being able to administer his own adrenaline. Even the most formidable attack may be averted by early treatment, and the asthmatic becomes by constant practice the best judge of his own condition. Among methods of administration, inhalation of 1 in 100 adrenaline from a fine spray has proved useful in aborting early attacks in individual cases; and the intramuscular injection of adrenaline in oil leading to a prolonged liberation of the active constituent has sometimes been effective. But when a patient has struggled on with his occupation in the face of increasing dyspnoea, and has delayed effective measures until too late adrenaline may lose its efficacy and 10 to 50 times the normal dose prove necessary, spread out over a number of hours. The time involved is a serious matter, for the patient should be under constant supervision.

Most asthmatics know by experience that hot coffee is an excellent palliative in the early stages of an attack, and as long ago as 1912 Pal showed that caffeine would reduce the bronchial spasm induced in guinea-pigs by peptone. It was subsequently found that caffeine also stimulates the medullary centres. Recently other purine derivatives have been used in the treatment of bronchial asthma, and theophylline seems the most efficient. In 1931 Hermann and Aynesworth successfully treated a refractory asthmatic with theophylline injected intravenously, and since then many other authors have had similar success. Thus Carr has treated 22 patients with status asthmaticus who were received as acute emergencies and who did not respond satisfactorily to adrenaline. In half of the cases 0.48 g. theophylline in 2 c.cm., given intravenously over 2 minutes, brought immediate relief. In the remainder the effect was evident within half an hour and lasted for a variable time, from one hour upwards. In 5 cases out of the 22 there was no recurrence: that is to say, a single injection had effected an immediate cure. In about one-third of the cases there were undesirable toxic reactions, such as dizziness, nausea, vomiting, 'pounding of the head', or pain in the chest; these were transient and unaccompanied by gross cardiovascular changes. No fatalities have been recorded, either here or elsewhere in the literature,

with this dosage. These results are most encouraging, though the exact mode of action of the theophylline is still under dispute. It has been suggested that it restores the sensitivity of the tissues to adrenaline in some unexplained way. It seems more probable that by a direct action on the bronchi and upon the medulla it breaks the vicious circle for a sufficient length of time for the patient to recuperate. While it is at present advisable to restrict the use of theophylline to the refractory cases until further experience has accumulated, it may well be that in the future it will prove to have a still more extended use.

### The Selective Action of Thio-Bismol on Induced Malaria

By M. D. YOUNG, S.D.

S. B. McLENDON, M.D.

and

R. G. SMARR, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXII, 19th June, 1943, p. 492)

1. THIO-BISMOL in 0.1 or 0.2 gm. amounts was found to have an inhibitory effect against *P. vivax* parasites which were half grown, i.e., about sixteen to twenty-eight hours after the last paroxysm caused by that brood of parasites. Parasites older or younger were not affected.

2. On examination of the blood, thio-bismol seemed to injure the half grown parasites and to reduce their numbers (density). No such effect was seen when parasites were older or younger.

3. By giving the drug during the sixteen to twenty-eight-hour period after a paroxysm, that series of paroxysms was eliminated. Thus paroxysms were converted from quotidian to tertian periodicity.

4. Paroxysms converted to tertian periodicity usually remained so during the remainder of the infection and sometimes through several subinoculations.

5. The occurrence of paroxysms every other day (tertian) instead of daily (quotidian) enables a neurosyphilitic patient better to undergo a full course of malaria therapy.

6. In *P. malariae* infections, a definite action of thio-bismol against any particular age group of the parasites could not be demonstrated. The administration of the drug sometimes gave temporary rest and a transitory diminution of parasites.

7. Practically no effect of thio-bismol could be demonstrated against *P. falciparum* infections. Neither the course of the paroxysms nor the parasite density was considerably altered by the administration of the drug.

8. For the termination of *P. vivax* infections it has been found that one injection of thio-bismol given the day quinine is started usually acts quicker than quinine alone by preventing a paroxysm the following day. It is suggested that this combination might find a wider use generally.

### New Advice on Gas Gangrene

(From the *Lancet*, i, 12th June, 1943, p. 745)

It is remarkable that in this fourth year of the war very few of our medical men in uniform have any first-hand knowledge of gas gangrene, which at material times in the 1914-18 war affected 1 to 10 per cent of the wounded, and which still has a fatality rate of 40 to 50 per cent. To improve our defective knowledge about this serious infection, the war wounds committee of the Medical Research Council produced in 1940 a useful memorandum on the subject, and a revised edition enlarged to twice the length of the original is now appositely issued. It deserves careful study by regimental medical officers, surgeons and pathologists. Gas gangrene is an infection of tissues, usually muscle, by anaerobic toxigenic bacteria

(*Clostridium welchii*, *Cl. septicum*, *Cl. oedematiens*) which with the exceptions of *oedematiens* invade the tissues already destroyed by their toxins. A knowledge of the conditions predisposing to gas gangrene will enable the medical officer to take early preventive action, and in the new edition these conditions are enumerated as extensive laceration of muscle as in compound fracture, obvious contamination of the wound with soil, clothing or other foreign body, interference with blood supply as by a tourniquet or a tightly packed dressing, severe shock and (perhaps most important of all) delayed surgical treatment. Infection is most likely in wounds of the buttocks and legs, and it is well to remember that insignificant entry wounds may be associated with much muscle necrosis. The regimental medical officer must also be familiar with the symptoms and signs of commencing gas gangrene—the local pain and swelling, the quickening pulse, the altered mental attitude—which indicate an urgent need for medical treatment.

Gas gangrene is a combination of toxæmia and local bacterial invasion; so both prophylaxis and treatment have the dual purpose of preventing bacterial proliferation and counteracting toxin production. Surgical excision of dead and dying tissue, about which the memorandum gives useful advice, is the most important single prophylactic; and it must never be unnecessarily delayed, for the incidence of gas gangrene rises steeply among wounds unattended for more than 24 hours. The surgical toilet should be supplemented by bacteriostatic drugs, both locally and systematically. For local use sulphanilamide alone or in combination with sulphathiazole is still the sulphonamide of choice, but local application will be relatively ineffective in unexcised and deep penetrating wounds. A trial might be given to the amino-acridines, such as proflavine, which experimentally are efficient in gas-gangrene infections. To counteract the bacterial toxæmia, polyvalent antitoxin is recommended, as soon as possible after wounding, for all casualties of the types likely to develop gas gangrene. Doses, for both prophylaxis and treatment, are three times the original dosage and are now more in line with that suggested in the *Lancet* primer on *Wound Infection*. The new insistence on the prophylactic use of antitoxin is welcome, for in many quarters it was being condemned without fair trial. In this the committee may have been influenced by recent experience in the Middle East where *oedematous* gas gangrene, which like tetanus is principally a toxæmia and unaffected by sulphonamide therapy, was the most common type of infection. Intravenous injection is recommended, which, if not so necessary for prophylaxis, is essential for the effective treatment of the incipient case. The clinical section ends with a number of questions that can be answered only by co-ordinated clinical and laboratory research, of which not the least important part is the careful recording of findings and treatment in every case of gas gangrene.

Compared with the original memorandum, this edition offers a much more detailed scheme for the isolation and identification of the gas gangrene group of organisms and other wound pathogens. Laboratory workers will find the notes up to date and very useful; they have been prepared by the Committee of the London Sector Pathologists and are largely the fruit of personal experiences. They would be even more valuable if short practical courses on the anaerobes could be arranged, at some of the listed reference laboratories, for both British and Allied pathologists.

### Albumin and Globulin Levels in Serum

(From the *Lancet*, i, 29th May, 1943, p. 688)

AMONG the less useful phrases learnt by the student, and used by him to annoy the examiner, and later the clinical laboratory, is 'reversed albumin-globulin ratio'. Kagan points out that this reversal by itself does not indicate any particular disease; and in a series of estimations on 345 patients shows that it may be

# BOVRIL AS AN AID TO NUTRITION

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In many illnesses, when gastric secretion is impaired and is deficient in hydrochloric acid, Bovril corrects this condition by restoring the normal volume and activity of the gastric juice, thus aiding the peptic digestion and absorption of protein foods.

In 1911, the late Professor Thompson, of Dublin, established that Bovril had the power of ministering to nutrition by the assistance it gave to the assimilation of other foods. Recently a remarkable series of experiments has been conducted at an English University. A group of medical students volunteered to undergo the unpleasant experience of allowing the passage of an œsophageal tube into the stomach so that accurate studies might be made of the effect of certain beef preparations. One of the substances investigated was Bovril.

As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril

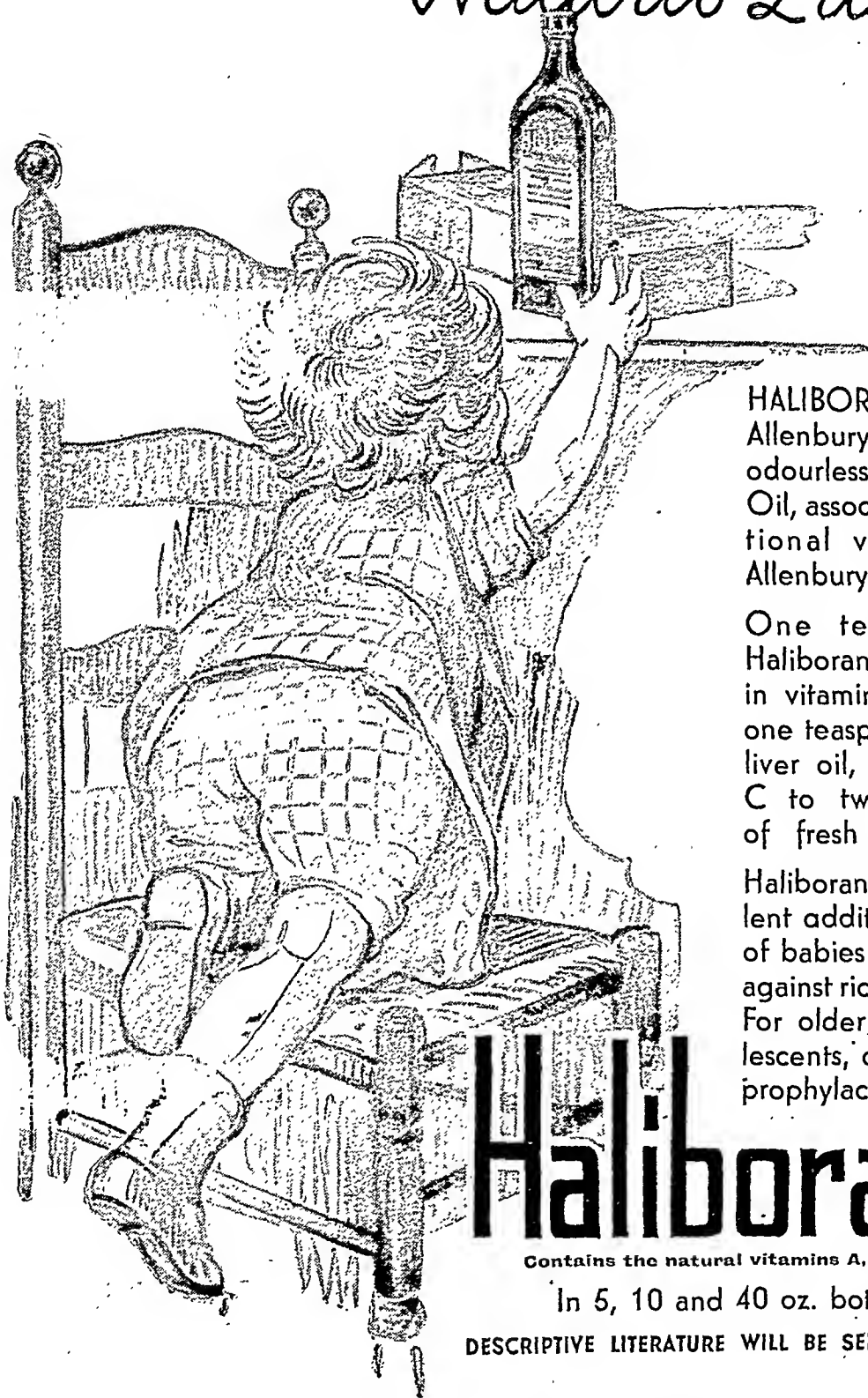
emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

Everyone, therefore, who is run down through strain or illness, or who feels in need of extra strength to cope with the demands of modern life, should take a cup of hot Bovril daily. It is a delicious and stimulating way of keeping fit and strong.

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due to excess of globulin reduction of albumin or a combination of both. Since a low globulin level has been noted only in prematurity, soon after severe hemorrhage and in advanced cirrhosis, it seems safe to assume that the globulin level is usually not reduced by disease, and any substantial variation is an increase. Three groups of cases were distinguished in his series:—

(1) Total protein above 7.5 per cent. Always due to increased globulin (9 per cent of his cases).

(2) Total protein below 7.5 per cent where the reduction was due solely to reduced albumin (65 per cent).

(3) Total protein below 7.5 per cent when albumin was reduced and globulin raised (26 per cent).

This last group included all forms of hepatic disease as well as neoplasm and heart failure, acute glomerulonephritis and a combination of diseases such as lymphogranuloma venereum, which gives a raised globulin, and malnutrition which gives a reduced albumin.

The reversal of the A : G ratio was noted so often and in so many diseases that its continued application is no longer justified. In most cases a total protein estimation should suffice, an increase being attributable to globulin and a fall to albumin. This could be brought out by a simple test for raised globulin, such as the formol-gel test or the globulin-precipitation test. Only in the small group of diseases in which albumin may be reduced and globulin simultaneously raised is there any justification for embarking on the more complex procedure of total albumin and globulin estimations.

### Health and Tonsillectomy

(From the *British Medical Journal*, ii, 11th September, 1943, p. 334)

A FEATURE of medical practice in recent years has been the popularity of tonsillectomy, especially among patients of well-to-do families; over half of the children in boarding schools have had their tonsils removed. Paton in his analysis of the data relating to 424 girls at boarding schools, of whom 42.9 per cent had a history of tonsillectomy, suggested that this operation was carried out too readily, and that the tonsillectomized group had no advantage over the group who were not operated on. Since this inquiry a mass of material has been collected by the School Epidemics Committee of the Medical Research Council. The data were based on the records of an average number per term of over 10,000 boys and 3,500 girls during 1930-34. Of the children studied 56 per cent of the boys and 50 per cent of the girls had had their tonsils removed. The sickness experience of the tonsillectomized group was no better than that of the children in whom there had been no operation; in fact, there was some slight indication that the incidence of rheumatism, otitis media, and mastoid disease was higher among the former. A comparison of the sickness incidence before and after the operation was made for a selected group of 364 boys who had their tonsils removed on the advice of the school medical officer. Before operation this group had an attack rate for nasopharyngeal infections which was 8.7 per cent greater than the expected rate obtained from age distribution and rates of all boarding schools combined. After tonsillectomy the attack rate was 0.5 per cent less than the expected rate. The committee concluded that in properly selected cases an operation was of real value, but in general it was performed for no particular reason and with no particular result.

A further contribution to the subject has been made by Paton, which extends his previous study to the decade 1930-39. The data are based on the records of 909 girls, of whom 57 per cent had had a tonsil-adenoid operation, compared with 43 per cent in the earlier study. The physique of the girls who had undergone operation was similar to that of the girls who had not been operated on, and girls of exceptionally low weight and height and above the average were as common in the one group as in the other.

Common colds were more frequent among the tonsillectomized than among the rest, the rates being 114 per cent and 97 per cent respectively. Influenza was also slightly more prevalent among the former group—43 per cent, compared with 39 per cent. Only a few cases of tonsillitis occurred during the ten years, the tonsillectomized group having a slightly better record with a rate of 1 per cent, compared with 5 per cent for the other group. All other cases of sore throat were as frequent in the one group as in the other, the rates being 40 per cent for those who had been operated on and 41 per cent for the remainder. Susceptibility to the common infectious diseases of childhood was about the same in both groups, 26 per cent of the tonsillectomized children and 24 per cent of the others contracting these diseases. There was a considerable difference between the two groups for bronchitis, the rate among the tonsillectomized being 27 per cent, while for the others it was only 16 per cent.

An interesting comparison was made of the experience of the girls who had tonsils only removed and those who had an operation for adenoids only. The rate for bronchitis and for otorrhoea among the group who had only their tonsils removed was 23 per cent and 0 per cent, while the rates for the other group were 4 per cent and 8 per cent respectively. The number of girls concerned, however—tonsils only 57, adenoids only 24—is too small for definite conclusions. The author suggests that the removal of tonsils is the factor in the combined operation which is responsible for the reduction in tonsillitis and for the increase in respiratory infections, while the removal of adenoids alone reduces the incidence of respiratory infections but increases the liability to attacks of otorrhoea. In the combined operation the removal of adenoids failed to counteract the increase in respiratory diseases which resulted from the removal of the tonsils. This study supplies additional evidence to support the view that a large proportion of the tonsil and adenoid operations in children are unnecessary, entail some risk, and give little or no return, while a reduction in their number would not have any unsatisfactory result and might, perhaps, be beneficial.

### Sweat Loss

(From the *New York State Journal of Medicine*, Vol. XLIII, 15th July, 1943, p. 1306)

IN seasons and regions of great heat and high humidity, profuse perspiration is a prostrating, although expected, phenomenon. Fluids of various kinds are thirstily imbibed to replace loss through excessive perspiration, without thought of whether the ingested liquid really replaced the lost fluids. Greater relief could doubtless be attained if the physiology and chemistry of sweating were better analysed and realized.

Sweat is a saline acid solution which may be shed at the rate of a liter an hour under trying circumstances.<sup>1</sup> It contains basic salts, especially sodium and potassium chloride, of which several grams may be lost on a hot, humid day. The acidity of sweat is largely determined by its content of lactic acid, which may be present in large amounts.<sup>2</sup> Nitrogenous substances are also excreted by sweat, and such excretion has been known to reach a total of several grams of nitrogen per day. Excessive sweating may result in the elimination of more alkaline chlorides by the skin than by the kidneys and tends to result in dehydration through such loss of salt and water. Thus a physiologic process can lead to collapse or to severe muscle cramps, which can, however, be relieved or averted by drinking not water but saline solution.

<sup>1</sup> Best, C. H., and Taylor, N. B. *Physiological Basis of the Practice of Medicine*, Second Edition, Baltimore, Williams & Wilkins Co., 1939, p. 1006.

<sup>2</sup> Peters, J. P., and Van Slyke, D. D. *Quantitative Clinical Chemistry*, Baltimore, Williams & Wilkins Co., 1939, Vol. I, pp. 271, 478 and 772.



Recently another important metabolic loss has been reported in cases of profuse perspiration. Water-soluble vitamins are excreted by sweat and excessive perspiration may cause an undue loss of such vitamins. It has already been demonstrated that ascorbic acid, thiamin, riboflavin, niacin, and pantothenic acid may all be eliminated in perspiration. As much as 10 per cent of some of these vitamins may be lost through this avenue of excretion. This is not a negligible amount if the diet is not optimal or, if there is a protracted period of heat, as in tropical regions.

It must be obvious that in the intense heat of summer or in the tropics it is not enough to drink extra water to replace the loss incurred through sweating. Mineral loss, particularly sodium and potassium chloride, must be replaced. It now also seems that the vitamin intake should be increased in certain instances to allow for losses sustained when sweating is excessive.

\* Cornbleet, T., Kirch, E. R., and Bergeim, O.  
J. A. M. A., 112, 426 (June 12), 1943.

### Blackwater Fever

By T. E. WILSON

(Abstracted from the *Medical Journal of Australia*, Vol. II, 20th November, 1943, p. 414)

A CASE of blackwater fever is reported in which the onset followed a course of 'Atebrin'. It is therefore suggested that blackwater fever is due to a hypersensitivity, not to quinine, but to a by-product liberated from the parasites by an antimalarial drug.

Although the urine remained black for more than three days, recovery occurred. The treatment employed consisted of alkalization of the urine, the administration of sufficient fluids by mouth and by the intravenous route to maintain a urinary output of an average of 97 ounces per day for the first five days, repeated blood transfusion, and the temporary avoidance of antimalarial drugs.

The sternal marrow of this blackwater fever patient is described. At the onset of the disease the sternal marrow picture was within normal limits but within three days there was great hyperplasia of the marrow affecting the pronormoblasts and the more mature cells of the definitive normoblastic series. With the cessation of the hæmolytic, the marrow picture gradually returned to normal. The disappearance of the parasites from the peripheral blood in this case of blackwater fever was accompanied by their absence from the sternal marrow.

#### ADDENDUM

Since submitting this paper for publication I have been fortunate in having under my care another patient suffering from blackwater fever! Perhaps the patient did not regard this as particularly fortunate. The report of the second case is appended here. In this case the urine was black or very deep red for six days, and a diuresis of 118 ounces of urine per day was maintained for the first twelve days; but it was necessary to give 21 pints of blood to restore the blood count to normal limits. Reactions after these transfusions were minimal. It is obvious that the filtration pressure in the kidneys must have been maintained within normal limits. Examination of the sternal marrow again revealed considerable erythroblastic proliferation; this reaction was apparently cut short by the repeated transfusions. For the first day the blood of this patient contained *Plasmodium vivax* organisms; but no *Plasmodium falciparum* organisms were found in the blood films while he was in hospital. At no time were parasites found in films of his marrow. Like the first patient in this report, this patient had lived in districts in which 100 per cent of the population contract subtertian malaria, and it is extremely unlikely that he escaped infection with the *Plasmodium falciparum*.

### Patulin in the Common Cold Collaborative Research on a Derivative of *Penicillium patulum* Bainier

By H. RAISTRICK AND OTHERS

(Abstracted from the *Lancet*, ii, 20th November, 1943, p. 634)

PATULIN is about equally bacteriostatic to both Gram-positive and Gram-negative organisms; it is much less active than penicillin against Gram-positive organisms but much more so against Gram-negative ones.

The bacteriostatic power of the substance is unaffected by the presence of serum or pus.

The phagocytic activity of leucocytes is unaffected by a 1 in 8,000 solution, but inhibited by a 1 in 2,000 solution.

The lethal dose for mice is about 0.5 mg. per 20 g. body-weight, whether the substance is given intravenously or subcutaneously. Subcutaneous administration produced necrosis at the site of injection.

During the first four months of this year, patulin was given a trial in the treatment of common colds which were prevalent at a naval establishment in the south-east of England. Solutions of the substance were sprayed into the nose or snuffed up from the hand.

The results obtained were encouraging, 57 per cent of the treated cases recovering completely within 48 hours, compared with only 9.4 per cent of the controls.

No ill effects were observed.

### Orthopædic Trends

(Abstracted from the *Lancet*, ii, 20th November, 1943, p. 642)

IN his presidential address to the British Orthopædic Association, Girdlestone discussed the influence of the orthopædic surgeon on the treatment of fractures. He urges the young orthopædist to cultivate first an intimate acquaintance with the ways and manners of the mesoblast. Between the fractured bone ends there lies not an inert coagulated lymph plug but living cells that demand blood if they are to survive; and strong skeletal traction strangles such cells. The osteoblast needs the stimulus of 'push' if it is to thrive—such stress, as Keith puts it, 'is as necessary for its health as exercise is for the living body'. For the fractured femur Girdlestone thus advises fixed extension on the Thomas splint with skin strapping in the old-fashioned way. Much has been written about the ingenuity of this Thomas splint, and Keith has pointed out how closely it follows nature's method of splinting. In vertebrates there is central bony support for the limb, whereas in crustacea and insects there is an ensheathing support. The Thomas splint is the sheath with unnecessary parts cut away; in the 'Tobruk' plaster, lately described by Buxton, plaster is used over the Thomas to complete the encircling sheath. When to move or not to move the difficult joint fracture is always a problem. Girdlestone advises early non-weight-bearing movements; thus in the knee, providing the limb is adequately slung, passive exercises can be started in 4 to 5 days, and active ones a few days later. For the fractured scaphoid adequate reduction is more important than union; he would place the wrist in full dorsiflexion for three months, observing the greatest gentleness in changing the plasters. He thinks the field for grafting the fractured scaphoid but a small one, seeing that even in practised hands the operation is neither always successful nor devoid of risk of carpal damage. Girdlestone painted rather an alarming picture of the Smith-Petersen pin ploughing its way through the femoral head's vascular system. He suspects the pin of being a potent killer of heads, and pointed out that it takes several years for an avascular head to be recast. The most important part of the treatment of the fractured femoral neck is reduction; after that it can be held by the Thomas splint and Pearson



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flexion piece with Balkan frame extension, and perseverance with this simple method may well give results comparable to those of the pin.

From his experience and wisdom Girdlestone added a warning against 'attractive' operations—surgical exercises more fittingly done on the cadaver. The warning is timely, for with modern illustration difficult technical procedures are made to appear simple, and the operator (alas, often the patient too) may find that between the seeing and the doing of the thing there is a hideous nightmare. A patient's implicit trust should not be betrayed by such ill-considered adventures. 'The surgeon we want for ourselves and our children is one who will not operate if he can attain his purpose by conservative means, and who prefers a safe and simple operation to one which is attractive to perform, though perhaps a little dangerous.' Girdlestone elaborated three freedoms in the treatment of the fractured limb—freedom from pain, freedom from pins, where possible, and freedom of the circulation, remembering the need for subsequent expansion. He might have added freedom of the patient from want. As Henry Cohen has said, 'there are no diseases, there are diseased individuals'. The interlocking of orthopaedics with the social services, home conditions, employment and compensation is now recognized as part of treatment.

### Carbarsone Treatment for *Balantidium coli* Infections

By MARTIN D. YOUNG

and

ROBERT BURROWS

(From the *Public Health Reports*, Vol. LVIII, 20th August, 1943, p. 1272)

In 1939, seven infections of *Balantidium coli* were reported at the South Carolina State Hospital (Young, 1939). Up until that time there was not a universally accepted treatment for this infection. These seven infections were treated with carbarsone; this report presents the results of the treatment.

and A. L.) a course of 1.0 gm. per day (two doses of 0.5 gm. each) for 10 days eradicated the infection.

Post-treatment examinations were made repeatedly for periods extending from one month up to 4 years. The absence of balantidia during the follow-up periods indicated a cure.

These seven infections, as far as can be ascertained by the authors, appear to be the largest group treated as yet in this country.

#### SUMMARY AND CONCLUSIONS

Carbarsone, in course totalling either 5 or 10 gm. in a 10-day period, was given to six cases of balantidiasis. After one or two such courses of treatment, the infections were eradicated as shown by repeated post-treatment examinations some of which extended over a 4-year period.

A seventh infection, which received less carbarsone than the other six, also disappeared.

Carbarsone appears to be an effective drug in the treatment of *Balantidium coli* infections.

#### REFERENCE

Young, M. D. (1939) .. Balantidiasis. *J. Amer. Med. Assoc.*, **113**, 580.

### Feasibility of Bacterial Warfare

(From the *Journal of the American Medical Association*, Vol. CXXII, 17th July, 1943, p. 810)

THE Geneva Disarmament Conference of 1932 considered bacterial warfare serious enough to prohibit its use. This action contributed to the popular fear of pathogenic micro-organisms as effective military weapons. To allay this fear come two timely reprintings of the classic paper by Col. Leon A. Fox of the U.S. Army Medical Corps, which summarize the current opinion of military experts.

Threatened introduction of new weapons or methods of warfare has often had to overcome opposition based on ethical, religious or humanitarian grounds. The early use of gun powder had to overcome opposition of this type. Military history, however, teaches that a weapon has never been abandoned for such reasons

TABLE

Dosages of carbarsone and results of treatment in seven infections of *Balantidium coli*

Patient	Number of doses	Dose in grammes	Daily dosage (grammes)	POST-TREATMENT OBSERVATIONS		
				Length in months	Number of examinations	Number positive
D. H.	20	0.25	0.5	48	3	0
J. T.	20	0.25	0.5	40	16	0
S. H.	20	0.25	0.5	1	2	2
First course ..	20	0.25	0.5	1.5	3	0
Second course*	20	0.25	0.5	6½	15	4
H. K.	20	0.25	0.5	40½	12	0
First course ..	20	0.25	0.5	4	7	0
Second course	20	0.25	0.5	48	13	0
E. A.*†	15	0.1 to 0.24	0.1 to 0.24	25	11	0
J. W.	20	0.50	1.0			
A. L.	20	0.50	1.0			

\* Died of causes unrelated to balantidiasis.

† Irregular treatment. Total of 22 gm. given in 15 doses over a 22-day period.

‡ Approximately.

Carbarsone in the amount of 0.25 gm. per dose, two doses per day given for 10 days, eradicated the infections in two (D. H. and J. T.) of the four patients so treated. In the two failures (S. H. and H. K.) the course was repeated and was successful. In one case (E. A.) receiving the drug in smaller amounts the infection disappeared. In the other two cases (J. W.

unless displaced by more effective weapons or until adequate countermeasures have been developed. Military history also reveals that epidemics were often the determining factor in past wars. In many campaigns contagious diseases caused such great loss of life and such large numbers of non-effectives on both sides as to lead to a stalemate. In other campaigns

great differences in the degree to which the two opposing armies reacted to such epidemics occurred.

The major military pests of the past have been the enteric fevers, typhus, bubonic plague and smallpox, with influenza, the pneumonias, malaria, measles, meningitis and syphilis playing a minor rôle. Popularly it is often assumed that these diseases would be particularly effective military weapons. However, fully virulent causative agents cannot be prepared in large quantities and cannot be introduced in adequate doses into the bodies of unprotected and non-immunized enemy populations. The essential problem of bacterial warfare from an offensive point of view is therefore the problem of mass production of military pathogens and of devising safe and effective methods of inoculating the enemy. The whole group of enteric infections, for example, could probably never be successfully used as instruments of warfare. Real epidemics of these diseases are traceable only to infected drinking water. While contamination of reservoirs and municipal storage tanks is militarily feasible, such contamination would be largely ineffective because of routine filtration or chlorination methods. Modern sanitary methods, therefore, should be adequate countermeasures against this type of bacterial warfare.

Among the respiratory infections, a number of maladies are serious enough to be effective if ways of using them can be devised. The two diseases of this group most frequently mentioned are influenza and meningitis. In neither disease could the infective agent be prepared in sufficient quantities, virulence or stability for military use. The meningococcus, for example, is so delicate that it rapidly dies when exposed for even a few hours to temperature much below that of the human body. The only feasible methods of introducing meningitis into opposite forces would be by human carriers. This would be hardly worth while, since any military aggregation of great size already has so many meningitis carriers (anywhere from 2 to 30 per cent) that the introduction of a few more carriers would be of little moment.

The use of insect-borne diseases has also been repeatedly mentioned in the press, bubonic plague being the most frightful example. Possibly airplanes flying low could drop recently infected rats on opponent terrains. Even this, however, would probably not start an epidemic. Plague has been more or less endemic as a rodent disease on our own Pacific Coast for over a generation, yet there have been no local human cases in this region sufficiently numerous to be designated as epidemic. Only 6 cases of plague developed in 1924 among European troops stationed in the Punjab, in spite of the fact that 500,000 cases developed in the indigenous population. Typhus also would be ineffective, since control of typhus is a question of louse control.

Tetanus, gas gangrene and anthrax have been suggested as particularly effective military pathogens, since they are caused by resistant, spore-forming bacteria capable of prolonged periods of viability without loss of virulence outside the animal body. These micro-organisms, however, do not produce epidemics even though they are of military interest as wound invaders. Effective methods of preventing and treating wound infections have been developed. Since wound invaders are omnipresent in nature, the indiscriminate distribution of a few additional wound invaders would not add appreciably to the present dangers of combat.

One of the commonest scares concerns the dissemination of 'deadly bacterial toxins', of which botulinus toxin seems to be the pseudoscientific favourite. True, 'an airplane can carry sufficient (botulinus) toxin to destroy an entire city', provided a carefully measured lethal dose of this toxin is administered orally, subcutaneously or intrarectally to each inhabitant of that city. The release of food materials contaminated with tremendous amounts of this toxin might conceivably cause a wholesale local destruction of rodents and sparrows. At most the number of human casualties would be negligible. Bacterial toxins like bacteria are readily destroyed by heat and are therefore inactivated

by cooking. They are wholly unsuited for use in shrapnel or other projectiles.

Bacterial warfare is often extended in popular literature to include the use of boll weevils, corn borers and other agricultural pests. Most of these pests, however, take several years to propagate and invade a sufficient terrain to be effective economically. This would violate one of the fundamental laws of military science, since it might merely interfere with post-war economics, reducing the ability of a conquered nation to pay indemnities.

Summarizing his argument, Colonel Fox concludes that there are 'practically insurmountable technical difficulties preventing the use of biological agents as effective weapons of warfare'. In this he confirms the previous opinion of numerous German bacteriologists, who five years before the first war were assigned the task of suggesting safe and effective weapons of bacterial warfare. Ehrlich, for example, replied that 'nothing [he] could suggest would be of more than a nuisance value to the enemy and might even be a source of danger to our own troops.'

It is hoped that Colonel Fox's paper will be as widely quoted in the popular press as have been the numerous frightening hypotheses that it contradicts.

## Dhobie Mark Dermatitis

By S. LIVINGOOD

A. M. ROGERS

and

T. FITZ-HUGH, Jr.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIII, 4th September, 1943, p. 23)

### SUMMARY AND CONCLUSIONS

1. Fifty-two cases of localized contact dermatitis occurred in one organization (20th General Hospital) following the wearing of clothes marked by native dhobies. This represented an incidence of 14 per cent of exposed persons. It varied in severity from slight erythema and itching to an acute vesicular and bullous patch of dermatitis with extension to other parts and 'id' manifestations which were incapacitating.

2. The brown or black liquid content or 'juice' obtained from the nut of the ral or bella gutti tree, used by the dhobies in marking clothes, has been identified as the causative agent.

3. Of previously affected persons, 80.5 per cent were positive to patch tests (1 to 4 plus) which duplicated under standard controlled conditions the exposure to marking fluid. The remaining 19.5 per cent were positive only when tested with marking fluid obtained from green nuts. Only 13.4 per cent of previously exposed but unaffected persons were positive to patch test (1 plus) and in this group all of the reactions were minimal. Marking fluid obtained from green nuts caused a higher percentage of positive patch tests and more pronounced reaction than fluid obtained from older (dried) nuts.

4. We are of the opinion that the dhobie mark is the probable cause of most cutaneous disease acquired from wearing dhobie laundered clothes.

5. We believe it most unlikely that cutaneous fungus infections are transmitted by clothing washed by dhobies and therefore urge that the use of the term 'dhobie itch' as a synonym for tinea cruris and epidermophytosis be discontinued. The term represents an erroneous concept and leads to error in diagnosis and treatment of certain cutaneous diseases seen in the 'land of the dhobie'. We have not seen an increase of cutaneous mycoses in a large group of men who have worn dhobie laundered clothes continuously during a three months' observation period.

6. The importance of 'dhobie mark dermatitis' as a cause of disability in American officers and men in this theatre is obvious.

7. We have designed this cutaneous disease 'dhobie mark dermatitis'.

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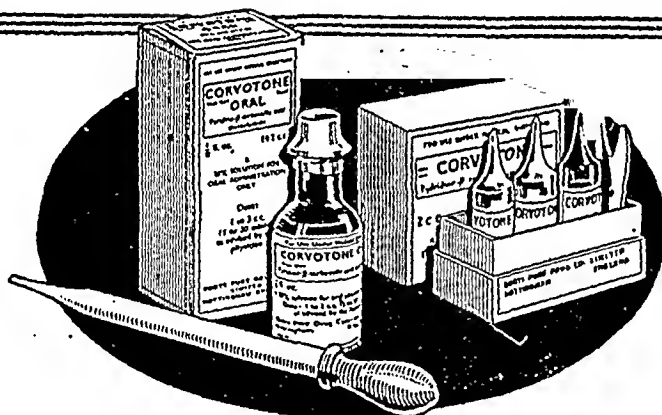


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## Immunization Against Tuberculosis

(From the *British Medical Journal*, ii,  
4th December, 1943, p. 716)

THE long and chequered history of attempts to immunize against tuberculosis is largely a record of failure. Subtract those attempts which were curative, leaving only those in the more rational and promising sphere of prevention, and the picture is less discouraging though much of it is questionable evidence. From the experimental point of view the facts are clear: it is perfectly possible to increase the resistance of animals to infection. Even a simple heat-killed vaccine will do this to some extent and perhaps dead vaccines prepared in other ways are somewhat better. A vaccine made from living but attenuated bacilli is more effective, and the mass of evidence testifying to the immunizing power of B.C.G. in animals is now overwhelming. Still more effective—for all this is a matter of degree—is a living vaccine made from Wells's vole tubercle bacillus, judging by the few experiments made by Wells himself in guinea-pigs and by the late Stanley Griffith and Dalling in calves before the war interrupted these studies. The degree of resistance achieved in these experiments was striking, amounting in calves almost to full immunity, and it encourages the liveliest hopes for the future of this method. Apart from its apparently greater efficacy, a vole bacillus vaccine has the important advantage that this organism is not a natural parasite of man or of cattle. Its virulence does not need to be artificially reduced, nor is there any danger of an increase in pathogenicity or of such a diminution as to reduce its immunizing power: it need only be maintained in its natural host to preserve its existing properties.

There is no *a priori* reason why these findings should not be applicable to man, and in fact human vaccination with B.C.G. has been extensively practised, though hardly at all in this country. Whether our indifference or disapproval is merited or not, the subject needs ventilation once more, and the Tuberculosis Association is to be congratulated on the meeting to discuss this matter which was held on 19th November: a report of its proceedings appears on p. 722. London is now probably the most cosmopolitan city of all time, and affords the opportunity of assembling speakers from many different countries without the travelling which must precede an international congress. This meeting was thus enabled to hear first-hand accounts of what is being done in Norway, Canada, and the United States; unhappily there was no representative of France. Norwegian achievements in the sphere of tuberculosis control are well known: we owe to them recognition of the fact that tuberculin-negative entrants to the nursing profession have a far greater liability to develop tuberculosis in the course of their training than the tuberculin-positive. The voluntary immunization of tuberculin-negative nurses with B.C.G. was begun as long ago as 1926, the vaccine being given subcutaneously and later intradermally. Among the vaccinated the annual incidence of tuberculosis has been 2.6 per cent and the mortality from it 0.2 per cent; the corresponding figures for controls (tuberculin-negative on entry and non-vaccinated) are 17.6 per cent and 1.8 per cent. Tuberculin-negative medical students have been given the same opportunity; the incidence of tuberculosis among the non-vaccinated has been 4.3 per cent and among the vaccinated 1.2 per cent. This effort has been by no means confined to these special classes of person. Although the Lübeck disaster caused an unfortunate and quite unmerited set-back in Norway as elsewhere, B.C.G. vaccination of the general public has been undertaken on an increasing scale since 1935, and the policy in 1940 was to vaccinate the whole tuberculin-negative population, including school children. That the German authorities now in control have stopped this programme will only serve, as Dr. Dedichen said, to increase its popularity when their occupation ceases.

No other country has such a record as this to show, nor are figures from elsewhere so significant,

though without exception they show the same trend. In Saskatchewan the programme of tuberculosis control described by Lieut.-Col. Bennett relies rather on segregation of infective cases, universal diagnostic facilities, and public education, but two interesting attempts with B.C.G. are in progress. Tuberculosis is still ten times commoner among North American Indians than in the European population; Indian babies are therefore being immunized, controls being provided by the simple method of inoculating only those born in alternate years. Immunization is also afforded to all tuberculin-negative nurses, among whom, as in Norway, the disease has in the past been unduly frequent. The results of these efforts, so far as they can yet be assessed, are satisfactory. These accounts of sustained and well-organized study, together with that given by Muckenfuss of experience in New York City, have no counterpart in anything which this country can produce. B.C.G. has recently been used here on a large scale, Col. Holst having immunized nearly 4,000 men in the Norwegian Army, but he had to obtain the material by air from Sweden. Lyle Cummins mentioned having obtained it from France, and treated only 12 patients when he was stopped by the Ministry of Health on the ground that 'the vaccine was not standardized'. It was more encouraging to hear from Dalling that the field experiments of the Ministry of Agriculture are now in progress on a large scale. The method has been to immunize calves, place them in heavily infected herds, and examine them post mortem only after natural death or at the end of their term of usefulness. Of 50 original animals, 20 have been killed so far, and of these only 3 had tuberculosis lesions, some being trivial: the present experiment embraces some thousands of cattle, but its results will not be known for 5 years or more. No calves have been immunized with a vole bacillus vaccine; a further series so treated should certainly be started. It was interesting to hear from Wells himself that he had administered living vole bacillus vaccine to 3 human volunteers; they became tuberculin-positive in consequence, and the only ill effect was a local abscess in one given a larger and possibly excessive dose.

A strong feeling was expressed at the meeting on 19th November that official inertia in this matter has lasted long enough, and, indeed, resolutions were passed the effect of which will be a request to the Ministry of Health that prophylactic immunization against tuberculosis should be at least countenanced if not encouraged. An official policy there certainly should be, and not merely a reluctance to embark on a difficult project until perhaps some of its difficulties have been removed by the greater enterprise displayed in other countries. It may be added that our other facilities for combating the disease do not compare so well with those in some other parts of the world that we can easily afford to disregard this one: an audible gasp at this meeting greeted the statement that in Saskatchewan there has been no sanatorium waiting-list for the past 15 years. If we are to await the full results of cattle tests, nothing will be done until 1950. To those familiar with Norwegian work in particular, it may well seem that the experimental period even in man is already over, and that nothing remains but to apply the method at whatever age, on whatever scale, and in whatever classes of person the circumstances demand. The case for at least a cautious trial in certain classes of hospital nurse is hard to gainsay if we assume a special liability to tuberculosis in that occupation. It is necessary for us to assume this because our information about the frequency of tuberculosis in nurses comes from Norway, Canada, New Zealand, and the U. S. A. No doubt a similar state of affairs, and the risks involved in admitting sputum-positive cases of pulmonary tuberculosis, diagnosed or not, to general hospital wards are now more widely recognized. But such an investigation has yet to be made and this is another matter in which an effort to overtake our hitherto more enterprising colleagues abroad might well be made in the near future.

## Reviews

**WAR WOUNDS AND INJURIES.** Second Edition. Edited by R. Malingot, F.R.C.S., E. G. Slesinger, O.B.E., M.S., F.R.C.S., and Ernest Fletcher, M.A., M.B., M.R.C.P. 1943. Edward Arnold and Company, London. Pp. vii plus 499. Illustrated. Price, 35s.

The title of this slender but expensive volume suggests that it has been designed to solve the problems which confront young surgeons responsible for the care of wounded in Casualty Clearing Stations and War Hospitals. This suggestion was sufficiently negated when the book fell open to the reviewer at page 65 which is occupied by a dissertation on the results of an experimental study conducted by Weddell, Guttman and Guttman into the recovery of pain-sensitivity in the intermediate zone in rabbits, and their conformity with the observations of Speidel on the nerves in the tail of the tadpole.

Closer study of the book makes it clear that it consists of a collection of unrelated monographs which are uneven in scope, quality and intention. The editors seem to have glimpsed this fact when they wrote in their preface that they had 'felt it best not to fetter the judgment of individual authors as to the scope or presentation of their articles'. As an earnest of this complete renunciation of all editorial prerogatives the senior editor himself has been allowed by his collaborators to mar an otherwise excellent section on chemotherapy by referring at length to conditions such as lateral sinus thrombosis and haematogenous osteomyelitis which are hardly in place in a book on War Wounds.

Lack of editorial supervision has led to much overlapping and some contradiction; for example, wound excision is dealt with under 'Treatment of Early Wounds', again under 'Wounds of the Chest Wall', where it apparently covers so heroic a measure as resection of the scapula by a paravertebral incision to expose its deep surface, again under 'Injuries to Blood Vessels' where 'proper coaption of deep tissues' is advised, and again under 'Compound Fractures' where it includes inspection of the fractured bone through a fresh and independent incision. The fact that excision is a prolonged and difficult operation is not mentioned anywhere. One-sixth of the whole book is devoted to peripheral nerve injuries, yet the author of another section (page 26) is allowed to advise the very doubtful expedient of marking the position of a divided nerve by a strand of salmon gut, the end of which is allowed to protrude from the wound. Many such defects could be quoted, yet the book contains excellent material and could be made both smaller and more useful. The article on abdominal injuries is full of information, but a busy and harassed junior surgeon would be grateful for a clearer presentation of the indications for laparotomy in abdominal and buttock wounds. It is good indeed to see the importance of post-operative dilatation of the stomach stressed at last in print.

The section on head injuries seems uncertain of its purpose. Only four of the 26 pages which it covers are devoted to treatment, and the advice given is too diffuse to be of any value to a young officer dealing with war casualties. To insist on the regular application (*sic*) of anti-gas gangrene serum gives a false impression of the frequency of gas infection in head injuries.

The article on compound fractures contains sections on joint injuries and amputations which might well have been omitted since both of these are dealt with elsewhere in the book. No mention is made of the fact that compound fractures which result from gun shot wounds show little tendency to shorten, and are easily over extended. Some of the operations advised are unduly extensive, for example, immediate excision

of the elbow joint for compound fracture of the lower end of the humerus.

In a war-time production one looks for austerity. Many illustrations could have been omitted without prejudice to the clarity of the text, and rhetorical statements such as that on page 26 concerning 'The silent witness to man's inhumanity to man' seem out of place. One's sympathies go to editors who attempt the production of works by multiple authors amid the difficulties and stresses of war, but this is not a good book.

J. G.

**THE MEDICAL ANNUAL: A YEAR-BOOK OF TREATMENT AND PRACTITIONER'S INDEX.**— Edited by Sir Henry Tidy, K.B.E., M.A., M.D. (Oxon.), F.R.C.P., and A. Rendle Short, M.D., B.Sc., F.R.C.S. Sixty-First Year. 1930. John Wright and Sons, Limited, Bristol. Pp. ix plus 432. Illustrated. Price, 25s.

The *Medical Annual* is now in its sixty-first year. It is a most valuable compilation. Here are given reviews each written by an eminent member of the profession of all the new publications of interest in his own particular subject, with references.

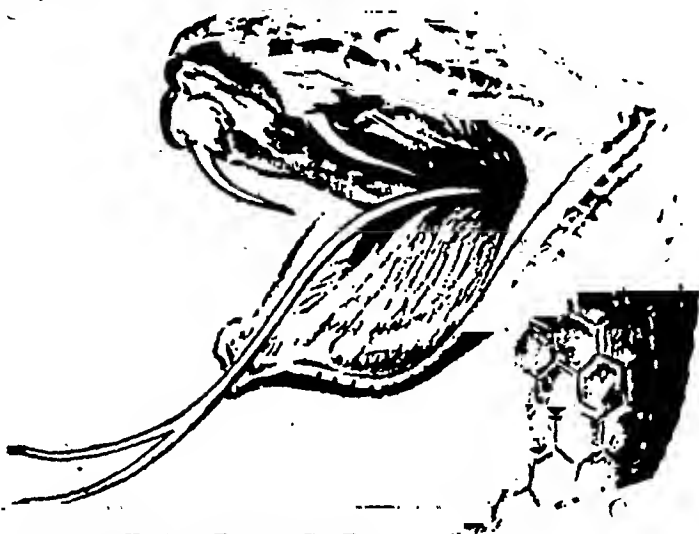
This book provides much the best method known to the reviewer of keeping in touch with recent developments in all branches of medicine. Of course in a book of 432 pages, much selection is necessary, and some selected subjects can be dealt with only briefly; but with the references, each contribution is of value and some are of great value.

The introduction contains the following two paragraphs:—

'The *Medical Annual* in recent years has reviewed a number of follow-ups of treatment of peptic ulcers from various parts of the world. It is striking how closely they agree with each other as to the ultimate results, the incidence of recurrences, and the relative results of medical and surgical treatment. It becomes clear that the best immediate results are obtained by gastro-enterostomy in duodenal ulcer. The relief is immediate and complete in a considerable percentage of cases, often lasts for many years, and the operation is attended with only a low mortality. It is not surprising that the doubts and protests of physicians were brushed aside by the surgeons for many years. Yet it is realized now that after effects are so serious and so frequent that the operation is generally regarded as unjustifiable, and has been practically abandoned. Indeed more than one distinguished surgeon spent his declining years in undoing the handiwork of his heyday.'

'Dangers of New Therapeutic Methods. Many new therapeutic methods have been introduced in the last 20 years, several of the highest efficiency. Any therapeutic method which is highly potent in the cure or alleviation of a disease must almost of necessity have power of producing toxic effects, and occasional catastrophes are unavoidable. Yet it is surprising to observe the recklessness with which a remedy introduced for a specific disease is used in conditions for which it is unsuitable or useless or even dangerous. When anti-diphtheritic serum was introduced 50 years ago, with its almost miraculous effects in diphtheria, the journals were full of communications claiming cures of all manner of conditions by its use. With no knowledge of allergy or anaphylaxis, tragedies occurred from its use in many trivial disturbances. The present *Annual* contains warning of at least three therapeutic measures. The dangers of sulphonamides are becoming more widely known but the various compounds are still employed uselessly, as for example sulphaguanidine in the treatment of ulcerative colitis or ordinary diarrhoea. Attention is also drawn to the need for care in the modern treatment of Addison's disease, where accidents have been known to occur from the use of ill-judged combinations of cortical extract, desoxy-corticosterone acetate, low potassium diet, and extra salt by mouth. Electro-convulsive therapy is now being employed on a considerable scale; the reviewer calls attention to

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 Ferri et Ammon citres grs. 5  
 Glycerini m. 6  
 Chittim grs. 24  
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 Gulanche grs. 12  
 Neem grs. 6  
 Myrabelans grs. 6



It has a tendency to become both chronic and quinine-resistant because it is usually complicated by malnutrition, weak liver function, protozoal and other intestinal infections; these combine to sap the patient's vitality and capacity for standing large doses of quinine. Pyrotone contains that something *extra* necessary for effectively combating Tropical Malaria. Besides quinine and other cinchona alkaloids it contains in addition reputed indigenous herbal remedies; diuretics; diaphoratics; iron and arsenic. These combine to render it unfailingly efficacious in combating recurrent attacks of fever in the most quinine-resistant cases. Thus Pyrotone eliminates malarial and intestinal toxins; prevents destruction of red blood corpuscles; remedies anaemia, reduces size of liver and spleen to normal; and restores the patient's general health within a very short time.

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\*Previous Editions were planned and edited by Lieut.-Col. Green-Armytage.

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various risks involved, and concludes that although it may for a time be the optimum available treatment in certain conditions, as a form of therapy it is crude, dangerous, and repellent to anyone who holds the central nervous system in respect.

In addition to giving reviews of publications appearing during the previous year, the medicine section of the *Annual* contains a number of interesting special articles covering certain subjects such as mass radiography for pulmonary tuberculosis, typhus fever, yellow fever and sciatica.

Surgical subjects discussed are very numerous, and many of the contributions are illustrated by excellently reproduced photographs (some being in colour) and diagrams, and of course war surgery occupies an important place.

An interesting minor point concerns fractured ribs:—*'Surgery of the Chest.*—The time-honoured treatment of fractured ribs by strapping the chest is being replaced by the much more effectual method of injecting a local anæsthetic, such as nupercaine or procain.'

A special article deals with ante-partum hæmorrhage, and another with blood and serum transfusion.

**ESSENTIALS. FOR FINAL EXAMINATIONS IN MEDICINE.**—By John de Swiet, M.D. (Lond.), M.R.C.P., Captain, R.A.M.C. Second Edition. 1943. J. and A. Churchill, Limited, London. Pp. viii plus 165. Price, 7s. 6d.

THE reviewers' first section to this booklet was unfavourable. How could a small book of 165 pages be of any real use? How could it do anything but encourage 'cramming', a deplorable procedure?

In the preface to the first edition the following sentences appeared:—

'The object of this little book is to provide students up for their "finals" in medicine with the means of rapid revision of the most important and most likely subjects which they may encounter in their papers. It is not claimed that anything like all the possible questions have been provided for, but the endeavour has been to make the selection representative of all the systems and their diseases. It is naturally assumed that the major textbooks have been gone through thoroughly, and therefore this book is chiefly intended for those who now wish to crystallize and summarize their knowledge.'

This edition has been thoroughly revised and all bacteriological and public health aspects have been omitted; a few common skin conditions and infectious fevers are discussed.

After reading much of the book, the reviewer feels that some of his doubts have been removed. The accounts of some diseases however are so condensed that their utility is rather doubtful. Used as the author intends it to be used, the book should be of value, but it seems rather likely that the book will be used in other ways. Nevertheless the reviewer is keeping this book for possible use by his son while studying medicine!

J. L.

**TROPICAL AND SUB-TROPICAL DISEASES (OXFORD WAR MANUALS).**—By C. H. Barber, D.S.O., M.A., D.M. (Oxon.), M.R.C.S., L.R.C.P., Lieut.-Col., I.M.S. (Retired). 1942. Oxford University Press, London: Humphrey Milford. Pp. xii plus 189. Illustrated. Price, 5s. Obtainable from Oxford University Press, Nicol Road, Bombay

This book was published in 1942 but has only recently reached us. It is apparently designed and written as a manual for medical officers proceeding from England to the tropics for the first time; its small size is intended to make it possible to carry it anywhere in the pocket. It contains only 188 pages including the index, and it deals with about 60 diseases, some of which might easily have been left out as they are either very rare or else unlikely to be seen by British medical officers, e.g. melioidosis of which only few cases have been recorded; espundia and tularæmia. Perhaps in writing on the latter two diseases the author

has the American market in view, but we hope that American readers will not regard this book as representative of British tropical medicine to-day, for it is in many ways inaccurate and often out-of-date.

The author writes about sunstroke, a condition which most authors consider as non-existent. His course of quinine treatment for malaria lasts for nine weeks and requires 640 grains of quinine. He recommends beginning malaria treatment by a purge of 3 grains of calomel 'to bring the temperature down (if malignant tertian) as soon as possible'. The prevention of relapse in malaria includes such procedures as applying locally to the spleen (*sic*) red iodide mercury ointment or iodine paint. Many statements made in the malaria section are rather inaccurate or misleading. Details are given of Field's method of 1940 of staining malaria parasites, but Field's much better method of 1941 is not given.

In other sections too, particularly those on kala-azar, dysentery, cholera and sprue, misleading or inaccurate statements are made. Some mortality rates quoted are far too high, e.g. cholera (untreated) 70 per cent, enteric fever in the tropics 30 to 40 per cent.

The author appears ignorant of the fact that 'sulphanilamide' is the name of a chemical compound and not the name of a group of drugs. He writes repeatedly of 'sulphanilamides'.

For immunization against yellow fever, the 'pantropic tissues virus vaccine' is recommended!

To deal with 60 tropical diseases in 188 pages means drastic selection and much condensation, but much more care should have been taken to see that the material included was accurate and in accordance with modern practice.

This is a very poor book.

J. L.

**A POCKET MEDICAL DICTIONARY.**—Compiled by Lois Oakes, S.R.N., D.N. (Lond. and Leeds). Assisted by Thos. B. Davie, S.A., M.D. (Liverpool), F.R.C.P. (Lond.). Sixth Edition. 1943. E. and S. Livingstone, Edinburgh. Pp. xx plus 451. Illustrated. Price, 4s. and postage 3d.

DOCTORS and nurses will remember how, when they were students, their teachers and their textbooks would often use words which they didn't understand; and how often they did not like to display their ignorance by asking the meaning of these words.

This little dictionary is designed to meet the situation. In a 450-page book of pocket size there is, in addition to a medical dictionary, information regarding degrees, diplomas, temperatures, weights, measures, tray preparations, first aid, poisons, physiological standards, examination of urine, stools, blood, etc.

Some of the terms given in the dictionary the reviewer has never heard or seen used, and out of the first twenty-six words there were eight with which he was completely unfamiliar; for example 'abiogenesis'. Is this a word which a medical student or nurse is likely to meet? Many other unusual words are also included. Some selection might make the dictionary smaller and handier.

On the whole however a very useful little book.

J. L.

## Correspondence

### INCOMPATIBILITY OF SULPHONAMIDES AND QUININE

SIR,—I have read with interest the note from a recent issue of the *Lancet* regarding the above, reported in the editorial columns of the *Indian Medical Gazette*, January 1944.

On this subject my observations are not the same as those of Dr. Niblock. I have on several occasions administered sulphapyridine with quinine ethylcarb without any visible uræmic symptoms. Each dose of



quinine and sulphapyridine was always preceded and followed by a dose of alkali with glucose mixture, and this I give as a routine when sulphonamides are administered. Adequate fluids are also advised. The simultaneous administration of any drug or food containing sulphur is only avoided.

Having no experience of any bad effect of the above combination up to this day and having 'no publication on this subject appearing in India', it seems to me that sulphonamide-quinine therapy (barring sulphonamide-quinine sulphate?) does not produce marked impairment of renal function, if adequate fluid is given along and no grossly excessive dosage of sulphonamide is administered. It is also known that in some cases sulphonamides alone give rise to uræmic symptoms. The impairment of renal functions in Niblock's cases might have occurred had sulphonamides been given alone.

It would, therefore, be interesting if members of the profession having facilities for investigation study the subject and communicate their findings through medical press for the guidance of general practitioners in this country, where occasions for sulphonamide-quinine therapy are not rare.

K. C. GHOSE, L.M.F.,  
Medical Officer, Redbank Tea Estate.

DAICHENG P. O.,  
JALPAIGURI DISTRICT,  
9th November, 1944.

[Note.—The above letter is printed exactly as it was received.]

The writer says that 'on several occasions' he has given quinine and sulphonamides together with no bad effects. Quite so. The danger may not be sufficiently great for the bad results to be seen in a small series of cases, but that fact does not prove that there is no danger. However in certain cases (e.g. a severe pneumonia plus a heavy malignant malaria infection) one may have to take a risk. (In the case quoted by the editor the malarial infection was moderate and was *P. vivax*, and there was no need to take the risk.) Moreover it should not be forgotten that some sulphonamides have some action in malaria.

With quinine and sulphonamides available, some doctors are tempted not to examine patients properly and make a correct diagnosis, but to prescribe both these drugs, feeling that if one does not act, the other will. Such a procedure is completely unjustifiable. With accurate diagnosis it should rarely be necessary to prescribe both, but we have so far seen no ill results in the few cases in which both have been given.

—EDITOR, I. M. G.]

## Service Notes

### APPOINTMENTS AND TRANSFERS

COLONEL B. C. ASHTON, V.H.S., is appointed Honorary Surgeon to the King, dated 6th March, 1943, *vice* Major-General A. A. C. McNeill, retired.

Colonel A. C. L. O's Bilderbeck, I.M.S. (retired), is appointed as Deputy Surgeon-General (A.R.P. including E.M.S.), Bengal, with effect from the 9th February, 1944.

Colonel H. Curran, on arrival in Bengal, is appointed as Civil Surgeon, Dacca, *vice* Major G. B. W. Fisher.

Lieutenant-Colonel D. P. MacDonald is appointed Officer on Special Duty in the office of the Director-General, Indian Medical Service, with effect from the 2nd February, 1944.

Lieutenant-Colonel H. H. Elliot, C.I.E., M.B.E., M.C., an Agency Surgeon, is employed as Chief Medical Officer and Inspector-General of Prisons in Baluchistan, with effect from the afternoon of the 5th February, 1944.

The services of Lieutenant-Colonel H. H. Elliot, C.I.E., M.B.E., M.C., are replaced at the disposal of the

Secretary to His Excellency the Crown Representative, with effect from the 6th February, 1944.

To be Surgeon to His Excellency the Viceroy  
Lieutenant-Colonel H. Williamson, O.B.E., I.M.S. (retired), 6th February, 1944.

Lieutenant-Colonel K. S. Fitch is appointed as Deputy Surgeon-General (Famine Relief Emergency), Bengal, with effect from the 9th February, 1944.

Lieutenant-Colonel H. W. Mulligan, Assistant Director, is appointed Director, Central Research Institute, Kasauli, with effect from the forenoon of the 14th February, 1944.

Lieutenant-Colonel P. L. O'Neill, on arrival in Bengal, is appointed as Civil Surgeon, Chittagong, *vice* Major J. Brebner.

Lieutenant-Colonel E. H. Lossing, on arrival in Bengal, is appointed as Civil Surgeon, Tippera.

Major L. M. Kelly, on arrival in Bengal, is appointed as Civil Surgeon, Faridpur, *vice* Dr. G. C. Sarkar.

Major G. B. W. Fisher, Civil Surgeon, Dacca, is appointed to be Surgeon Superintendent, Presidency General Hospital, Calcutta, *vice* Lieutenant-Colonel J. C. Drummond.

Major J. H. Caverhill, Civil Surgeon, 24-Parganas, is appointed as Civil Surgeon, Mymensingh.

Major J. Brebner, Civil Surgeon, Chittagong, is appointed as Civil Surgeon, 24-Parganas, *vice* Major J. H. Caverhill.

The undermentioned officer of the I.M.S. is seconded for service in the I.A.M.C.:—

Major J. P. J. Little. Dated 4th January, 1944.

The undermentioned officer of the I.M.S. reverts from the I.A.M.C. to Civil (Punjab):—

Major C. F. Garfit. Dated 24th December, 1943.

LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commissions)

To be Captains  
18th October, 1942

A. W. Howarth. P. R. W. Leigh.

Fazl-i-Haque. Dated 1st September, 1943.

Samuel Sindha Ramsingh. Dated 14th December, 1943.

Jambuswami Vaidhianadhan. Dated 17th December, 1943.

Ahmed Mohiuddin. Dated 12th January, 1944.

A. S. Johnson. Dated 1st November, 1943.

H. P. Banerjee. Dated 12th November, 1943.

20th November, 1943

P. K. Topa. H. Lakshminarayana.

P. Sharma. Dated 27th November, 1943.

20th December, 1943

B. C. Chatterjee. K. B. Das.

M. P. Patel. Dated 24th July, 1943.

R. V. Waingankar. Dated 15th December, 1943.

Harry Munro Archibald. Dated 13th January, 1944.

14th December, 1943

M. A. R. Khan. V. P. Jacob.

A. Mohmad:

14th January, 1944

H. D. Kapadia. S. C. Maitra.

S. H. Khan. Dated 15th January, 1944.

B. N. Chatterjee. Dated 16th January, 1944.

K. N. H. Rizvi. Dated 18th January, 1944.

J. N. Samadder. Dated 19th January, 1944.

To be Lieutenants

A. W. S. Webster. Dated 27th June, 1943.

S. N. Sahibzada. Dated 13th November, 1943.

14th November, 1943

S. L. Khosla. Akhunzada Mohammad

A. A. Awan. Yusuf.

K. D. K. Sherwani. Omer Yacob.

M. Singh. Gandharve Singh Sarin.

B. S. Sidhu. Jagjit Singh.

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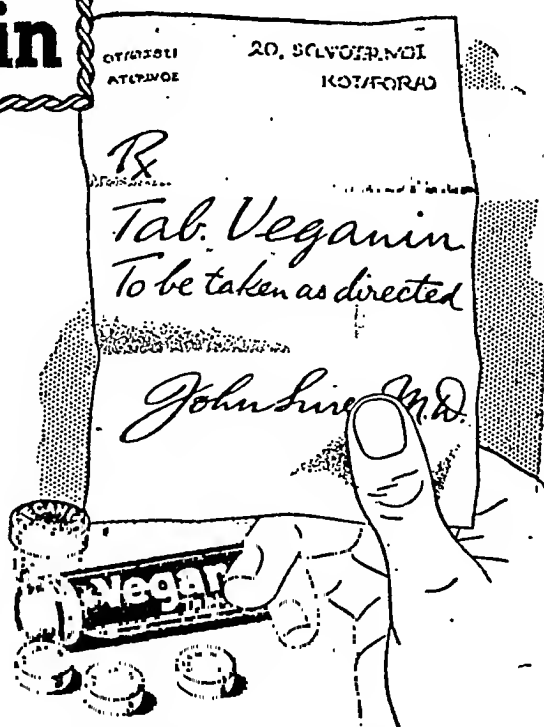
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 Mohd. Ghias-Ud-Din. Dated 19th November, 1943.  
 Pathpalli Sarvothamyya. Dated 11th December, 1943.  
 Sushil Kumar Das Gupta. Dated 20th December, 1943.

V. B. Naidu. Dated 19th November, 1943.

14th December, 1943

M. A. Chowdhury. S. N. Ghei.  
 J. Harinarain. Dated 8th January, 1944.  
 C. R. Rangoji Rao. Dated 19th November, 1943.  
 V. N. Vadawkar. Dated 21st December, 1943.

The undermentioned officers retire with gratuity and are granted emergency commissions from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
 (Short Service Commission)

12th January, 1944

Capt. I Singh. Capt. N. D. P. Karani.

To be Lieutenants

14th September, 1943

Prafulla Kumar Chatterji.  
 Govinda Pallab Ghose.  
 Sunil Kumar Sen.  
 Jagannath Chatterjee.  
 Bhupaty Banerjee.  
 Jitendra Chandra Chatterji.  
 Dilip Kumar Roy Choudhury.  
 Harisaday Chakravarty.  
 Sunilchandra Datta.  
 Amal Kumar Datta.  
 Pratul Chandra Sinha Roy.  
 Praphulla Kumar Chakravorti.

Ajit Kumar Biswas. Dated 13th November, 1943.

20th December, 1943

Mahesh Chandra Gupta. Suresh Kumar Kochhar.  
 Mohammad Kabeer Hashmi. Dated 19th January, 1944.

15th September, 1943

Sadr-ul-Islam Mohammad Golam Mannan.  
 Kazi Abul Monsur. Manik Ratan Sarkar.

14th October, 1943

Ajit Kumar Ray. Sisir Kumar Ray.  
 Sankar Prosad Das Gupta. Dated 8th November, 1943.

Dilip Kumar Mitra. Dated 10th November, 1943.

20th November, 1943

Sambhu Nath Datta. Shishir Kumar Ghose.  
 Harish Chandra Chakravarti.

30th November, 1943

Prabhat Kumar Bose. Sourindra Nath Sen  
 Gupta.

Ramendra Nath Dutta.

Subimal Chaudhuri. Dated 20th November, 1943.  
 Bimalendu Sen Gupta. Dated 14th December, 1943.  
 Aviot Thomas John. Dated 17th December, 1943.  
 Prem Raj Govind. Dated 19th December, 1943.  
 Jagat Narain. Dated 4th January, 1944.

(WOMEN'S BRANCH)

To be Captains

(Miss) Freda Emilia Freitas. Dated 11th December, 1943.

(Mrs.) Mathurabai Bhawanishankar Kagal. Dated 16th December, 1943.

(Miss) Lalitha Krishnarau. Dated 13th January, 1944.

(Miss) Lucy Aehamma Verghese. Dated 15th January, 1944.

(Miss) Mary Isaac Judah. Dated 18th December, 1943.

(Miss) Saradadevi Subbarao. Dated 8th December, 1943.

(Miss) Shireen Ardesbir Lal. Dated 2nd January, 1944.

(Miss) Roshan Nusserwanjee Chinoy. Dated 17th January, 1944.

To be Lieutenants

(Miss) Tehmina Namdar Irani. Dated 26th November, 1943.

(Miss) Munawar Sultana Sheikh. Dated 6th January, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
 (FOR SERVICE WITH THE INDIAN AIR FORCE)

(Emergency Commission)

To be Captain

Gour Gopal Chatterjee. Dated 4th November, 1943.

INDIAN LAND FORCES  
 SECONDED TO INDIAN AIR FORCE

(Emergency Commission)

To be Lieutenant

Deb Kumar Ray Chaudhuri. Dated 14th November, 1943.

The undermentioned officer of the I.M.S. reverts from the I.A.M.C. and is seconded for service with the Royal Indian Navy :—

Major W. Mackie. Dated 12th January, 1944.

The undermentioned officer of the I.M.S. (E.C.) reverts from the Royal Indian Navy and is seconded to the I.A.M.C.:—

INDIAN LAND FORCES  
 (Emergency Commission)

Capt. N. J. Choksey. Dated 2nd December, 1943.

INDIAN LAND FORCES  
 SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY  
 (Emergency Commissions)

To be Lieutenants

P. R. Sondhi. Dated 6th February, 1943.

C. M. Dave. Dated 27th March, 1943.

PROMOTIONS.

Majors to be Lieutenant-Colonels

M. K. Afridi. Dated 1st February, 1944.

G. S. Chawla. Dated 9th February, 1944.

INDIAN LAND FORCES  
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
 (Emergency Commissions)

Captains to be Majors

V. W. Clifford. Dated 28th February, 1944.

B. M. Pattanayak. Dated 21st November, 1941.

L. N. O'Hara. Dated 6th September, 1943.

C. B. Miller. Dated 13th February, 1944.

A. S. Rao. Dated 17th February, 1943.

INDIAN MEDICAL SERVICE  
 (Permanent Commissions)

The undermentioned officers (on probation) are confirmed with effect from the dates specified :—

Captain D. J. P. Spillane. Dated 9th January, 1939.  
 10th January, 1939

Captain J. M. M. Drew. Captain J. A. Anderson.  
 Captain A. M. Maekenzie. Dated 12th March, 1939.  
 Captain J. L. M. Whitebread. Dated 12th March, 1939.

Captain W. S. Hacon. Dated 12th May, 1939.

INDIAN LAND FORCES  
 SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
 (Emergency Commissions)

Lieutenants to be Captains

D. G. R. Fox. Dated 17th July, 1943.  
 M. A. N. Iyengar. Dated 29th September, 1943.

S. N. Basu. Dated 11th December, 1943.  
 N. Narasimhan. Dated 1st January, 1944.  
 J. J. D. Lobo. Dated 2nd January, 1944.  
 C. W. McNamara. Dated 3rd January, 1944.  
 S. W. W. Terry. Dated 4th January, 1944.  
 B. C. Chatterjee. Dated 7th January, 1944.  
 K. R. Kunjan. Dated 12th January, 1944.

17th January, 1944

P. C. Sarkar. U. K. Das Gupta.  
 G. C. Sen Gupta. S. B. Palit.  
 N. D. W. Morrison. Dated 16th January, 1944.

17th January, 1944

M. R. Rao. S. R. Rao.  
 J. S. Rao.

19th January, 1944

M. K. Sarkar. T. P. Bhadra.  
 S. N. Sen. A. L. Mukherji.  
 D. Bose. D. H. Robertson.  
 E. R. MacFarlain. Dated 21st January, 1944.

22nd January, 1944

S. N. Basu. N. N. Chatterjee.  
 V. B. Tawadey. Dated 24th January, 1944.  
 A. Satyanarayana. Dated 26th January, 1944.

27th January, 1944

S. B. Datta. P. S. Rao.  
 A. C. Sarkar. Dated 28th January, 1944.

1st February, 1944

K. D. Malviya. F. G. Orton.

2nd February, 1944

B. L. Verma. V. S. Joshi.  
 C. D. Torpy. Dated 5th February, 1944.

6th February, 1944

K. E. Tanner. E. R. White.  
 D. C. Mayberry.  
 A. H. Awan. Dated 8th February, 1944.  
 L. C. Emmett. Dated 10th February, 1944.

12th February, 1944

G. Mookerjee. E. P. O'Neil.  
 B. J. Pereira. D. S. B. Stephens.

13th February, 1944

G. S. Grewal. Satya Prakash.  
 A. Majid. M. H. Qamar.

13th February, 1944

A. Mahmood. A. S. Nagpal.  
 B. Singh. B. Uddin.  
 A. Din. S. M. H. Jafri.  
 G. R. Athwal. D. P. M. Datta.  
 J. H. F. Manekshaw. M. K. Bodas.  
 A. N. Lakhotia.  
 E. B. Naug. Dated 21st February, 1944.

22nd February, 1944.

K. K. Dhar. A. M. Lopes.  
 C. S. Prasad. Dated 24th February, 1944.

26th February, 1944

A. N. Datta. A. W. M. Garrad.

27th February, 1944

A. S. Bhasin. S. K. Jetley.  
 U. S. Notyal.  
 V. A. Sales. 28th February, 1944.

(WOMEN'S BRANCH)

(Miss) E. S. Chaube. Dated 4th January, 1944.  
 (Miss) S. I. Jacob. Dated 20th January, 1944.  
 (Miss) Dorothy Balraj. Dated 9th February, 1944.

(WITHIN INDIAN LIMITS)

*Lieutenant to be Captain*

B. B. Gupta. Dated 23rd February, 1944.

*Lieutenants to be Captains*

(SECONDED FOR SERVICE WITH THE INDIAN AIR FORCE)

M. K. Mookerjee. Dated 1st February, 1944.

R. Jayaram. Dated 3rd February, 1944.

G. N. I. Venkatraman. Dated 4th February, 1944.

13th February, 1944

M. Hussain. M. R. Mahmood.

M. S. Maini. S. A. Hasnain.

K. Kurian. Dated 23rd February, 1944.

(SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY)

*Lieutenants to be Captains*

P. R. Sondhi. Dated 13th July, 1943.

C. M. Dave. Dated 18th August, 1943.

RETIREMENTS

Lieutenant-Colonel J. C. Pyper, O.B.E. Dated 18th March, 1944.

Major T. A. Malone retires on account of ill health. Dated 9th August, 1943.

The following retirement, with gratuity, is permitted :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

(Short Service Commission)

D. D. Verma. Dated 1st February, 1944.

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## Original Articles

### INFLUENCE OF MILK POWDER ON FLUORINE INTOXICATION IN RATS

By S. C. PILLAI  
R. RAJAGOPALAN

and

N. N. DE

(Department of Biochemistry, Indian Institute of Science, Bangalore)

DURING recent years, a considerable amount of evidence has been adduced by a number of workers that the dental defect known as 'mottled enamel' and also certain changes in bones, which are endemic in many parts of the world, are caused by the toxic action of fluorides present in the drinking water supplies of those areas (Smith *et al.*, 1931; Smith and Smith, 1932; Shortt *et al.*, 1937; Pillai, 1938; Wilson, 1939). The occurrence and distribution of fluorides in waters and in edible foods, as also their toxic effects, have been reviewed extensively (McClure, 1933; DeEds, 1933; Roholm, 1937; Greenwood, 1940). Attempts have also been made to remove the fluoride from the water supplies and to eliminate, or at any rate to mitigate, the adverse effect of that halogen. While such attempts have not so far met with any considerable measure of practical success, valuable observations have been recorded.

It is generally observed that the incidence and severity of fluorine intoxication have a definite relation to the economic and nutritional status of the communities. In India and elsewhere, it has been observed that in the particular areas of endemic fluorosis it is the people of the poorer classes that are most adversely affected. The diet of poor people, at any rate in India, consists mainly of starch with little protein and other important items. A diet rich in calcium, phosphorus and vitamin D is reported to have a beneficial influence on fluorine intoxication (Smith *et al.*, 1935; Roholm, *loc. cit.*). 'Pronounced C avitaminosis' has been considered a contributory factor in the production of severe chronic fluorine intoxication in man (Pandit *et al.*, 1940). With large intake of fluorine, a negative calcium balance has been found to take place (McClure and Mitchell, 1931), and in such circumstances it has been suggested that the fluorine monopolizes the calcium of the organism (Roholm, *loc. cit.*). The protective action of high calcium diets against the toxic action of fluorine has been noted by Lawrenz and Mitchell (1941). In the experiments of Ranganathan (1941), in which calcium was found to produce a mitigating influence on fluorine poisoning in rats, over 30 times the amount of calcium required for combination with fluorine to form calcium fluoride had to be

given; smaller amounts of calcium did not have the same protective effect. The addition of calcium hydroxide to fluoride-containing water in quantities calculated to precipitate the fluoride was not found efficacious in checking the occurrence of the mottled condition of the teeth in rats (Pillai, 1942). The administration of calcium salts mitigated the symptoms of fluorine intoxication in farm animals (Majumdar *et al.*, 1943).

Calcium has been assumed to act by combining with fluorine to remove it as the insoluble salt. But it is not clear why sometimes a very much larger amount of calcium than that estimated, on a stoichiometric basis is necessary for producing a mitigating effect. A further important query is whether the external symptom of mottled enamel is to be regarded as an indication of fluorosis of bones. There is considerable evidence that a relatively low intake of fluorine by rats and humans results in no measurable interference with calcium metabolism as determined by balance experiments, although it produces a marked effect on the enamel of the teeth even when no other symptoms of fluorosis are present. Evidence is also accumulating that 'fluorine exerts a direct local action on enamel-forming cells, and that the changes observed in the enamel and dentin are not produced primarily by changes in the blood calcium or phosphorus or disturbances in the parathyroids' (Schour and Smith, 1934, 1935). It would therefore appear that although the dental fluorosis and fluorosis of the bones are primarily due to fluorine poisoning, the mode of action of the causative element in the production of the two conditions may not be identical. It may perhaps be possible to induce by experiment a condition in which, while the mottled enamel may persist, fluorosis of the bones may not have developed at all. Such a result may be regarded as being of considerable practical value, for, although the mottled enamel is undoubtedly a form of disfigurement, fluorosis of the bones is a much more serious condition.

The object of the present inquiry, therefore, was to study the gross effects of certain types of diets, and to determine whether any of them could eliminate the more painful symptoms of fluorosis irrespective of the development of mottled enamel. The results have shown that, with a certain type of diet, the more serious symptoms of fluorosis could be eliminated to a considerable extent, though it was not possible to prevent the mottling of teeth. The experiments were carried out with young albino rats, and the observations made are described in this communication.

#### Experimental

At the start of the experiment the animals were about five weeks old and of about the same weight. They were divided into five groups, and they received different types of diets as indicated below.



The first set of animals (A) (see figures 3 and 4, plate XI) to serve as general controls was placed on a diet consisting of wheat flour, butter fat, cane sugar, common salt, vegetables, shark-liver oil, marmite and milk (also meat, twice a week); tap water was used for purposes of mixing these constituents and for the animals to drink.

The second set (B) (see figure 9, plate XII) to serve as specific controls was placed on a similar diet, but milk was excluded, and instead of tap water, distilled water containing sodium fluoride was used; each rat in this set was daily given 6 mg. of sodium fluoride in the water.

The third set (C) (see figures 7 and 8, plate XII), the fish-diet series, was put on a diet similar to that for the second set (B) but including fish powder; the fish used was a local variety, 'karwa', which was freed from bones before it was dried and powdered.

The fourth set (D) (see figure 10, plate XII), the egg-diet series, was put on a diet similar to that for (B) but including fresh whole fowl's egg.

The fifth set (E) (see figures 5 and 6, plate XI), the klim-diet series, was put on a diet similar to that for (B) but including the whole milk powder, klim.

*Composition of the fish powder, egg and klim*  
(Expressed as percentage)

Substituted for milk	Protein	Fat	Calcium	Phosphorus
C. Fish powder	80.76	6.12	0.10	0.14
D. Fresh egg (containing 75 per cent moisture).	13.40	10.50	0.07	0.22
E. Klim	26.70	28.00	0.82	0.62

*Observations on the animals.*—The rate of growth of a typical rat in each of the series is graphically represented in figure 1. Observations on the general condition of the rats in the different series, and on the average increase in the weight of the animals for the first four weeks,

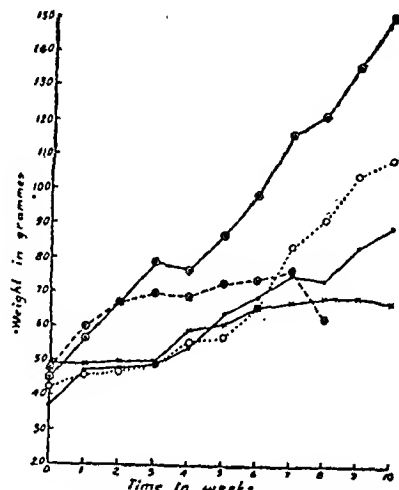


Fig. 1. The rate of growth of a typical rat under each treatment  
○—○ General control  
×—× Specific control  
— Fish diet series  
●—● Egg diet series  
■—■ Klim diet series

as also records of the gradual appearance of the external symptom of mottling of teeth are given in table I.

Four weeks after the above treatment, the concentration of sodium fluoride in the water used for the experimental animals was brought down to 10 parts per million since the condition of the animals in the series B, C and D was becoming worse (and also since the concentra-

TABLE I

Treatments	General condition of the animals during the first four weeks	Average weekly increase in the weight of the rats (gm.)	Appearance of mottled condition
A. General controls ..	All alive, normal and healthy	15	
B. Specific controls ..	After about a week the animals showed considerable difficulty in free movement, the limbs having been apparently stiffened and cramped; occasional bleeding of the nose was also observed; one became very ill and died after 17 days.	9	During second week.
C. Fish-diet series ..	Similar to above	14	During third week.
D. Egg-diet series ..	Similar to above	20	During third week.
E. Klim-diet series ..	All alive, normal and healthy	34	During fourth week.

Three rats were used for each of the control series and four rats for each of the experimental series. The growth rate of the animals and also the condition of the teeth were studied from time to time. Radiographic examination of the bone system was also carried out.

tion of the fluoride employed in the experiment was very much greater than that seen in the waters from areas of endemic fluorosis; the higher concentration of fluorine was initially employed for quicker development of the symptoms in the experimental animals). The

observations made two weeks after this modified treatment are recorded in table II.

pictures and other photographs of the animals are given in plates XI, XII and XIII.

TABLE II

Treatments	General condition of the animals	Average weekly increase in the weight of the animals (gm.)	Condition of mottling
A. General controls ..	All alive, normal and healthy	11	Persisting.
B. Specific controls ..	Stiffening and cramping of the limbs continued.	3	
C. Fish-diet series ..	The above symptoms persisted and two rats died, one after 30 days and the other after 37 days.	6	Persisting.
D. Egg-diet series ..	The above symptoms persisted and one rat died after 30 days.	9	Persisting.
E. Klim-diet series ..	All alive, normal and healthy	22	Persisting though less than above.

*Influence of a supplement of bone powder to the diets of animals.*—As a measure of further treatment, the diets of animals were improved. To the diets of one or two rats surviving in each of the series including those in A and C, for purposes of comparison, was added 0.5 gramme of bone powder per rat per day. The bone powder employed contained 17.5 per cent protein, 30 per cent calcium (CaO), and 25 per cent phosphorus ( $P_2O_5$ ).

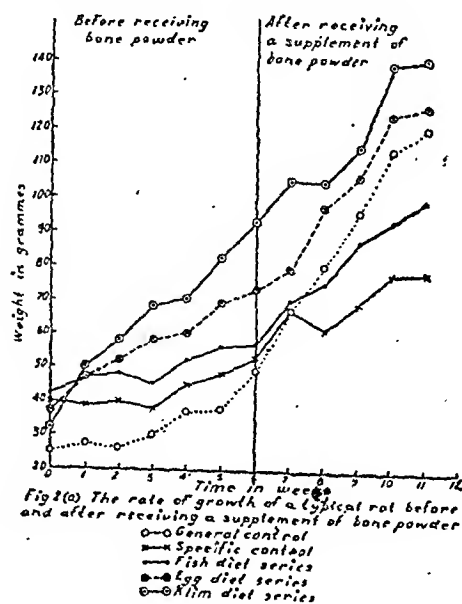
The supplement of bone powder brought about considerable improvement in the general condition and the growth of the animals suffering from fluorine intoxication; the stiffening and cramping of the limbs of the animals in the series C and D were relieved considerably, and their rate of increase in weight rose markedly. At this stage there was, in general, considerable improvement with regard to the symptoms of mottled enamel also. The reduction of concentration of fluorine in the water and the influence of diet have been of course important factors in the production of the latter effect. Apart from these and other considerations, the rat incisors would appear to be very peculiar. Smith (1935) observed that 'the lower incisors of the rat completely renew themselves every 30 days. Normal enamel areas alternate with the areas of defective calcification, the extent of which corresponds with the interval between the eruptions'.

In the case of the rats in the klim-diet series (E), however, there was no special benefit produced by the supplement of bone powder; even without the supplement of bone powder, it was of interest to observe that the radiograph of their bone system was practically identical with that of animals receiving no fluoride.

The foregoing observations are given in table III and figures 2a and 2b. The x-ray

TABLE III

Treatments	Average weekly increase in the weight of the animals before and after the addition of bone powder to their diets (gm.)	
	Before the addition of bone powder	After the addition of bone powder
A. General controls ..	5	14
B. Specific controls ..	3	5
C. Fish-diet series ..	3	9
D. Egg-diet series ..	5	11
E. Klim-diet series ..	9	6



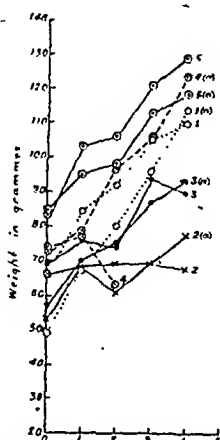


Fig. 2(b) Comparative growth rate of rats with and without supplement of bone powder

1. General control	1(a) With bone powder
2. Specific control	2(a) " " "
3. Fish diet series	3(a) " " "
4. Egg diet series	4(a) " " "
5. Klim diet series	5(a) " " "

### Summary and conclusions

The inclusion of sufficient quantities of whole milk powder (klim) in the diets of experimental rats afforded remarkable protection against fluorine poisoning in the animals.

A supplement of bone powder also brought about considerable relief from fluorine intoxication in the experimental animals.

The beneficial influence of 'klim' and of bone powder may be due to their calcium as also their phosphorus contents in organic combination. Whether it is largely a question of the quantity of available calcium or of the calcium-phosphorus ratio has to be ascertained by further experiments which are in progress. The relative importance of calcium and phosphorus in relation to fluorosis is also under study. At the same time it may be observed that there is a demand for phosphorus in foods at least as high as or higher than that for calcium. In the adult, if phosphorus is lacking in the diet, the body can draw upon its apatite quarry of the bones for the lacking element; in growing animals this is not possible and a low phosphorus intake limits growth. There is an optimal relation between calcium and phosphorus in the diet which is about 1 : 1 or possibly 1 : 1.5. It is known that in rats a high calcium-low phosphorus ratio and a low calcium-high phosphorus ratio both limit the rate of growth and, in the absence of vitamin D, conduce to rickets. In milk the ratio of calcium to phosphorus is as 1.27 : 1. Sherman's suggestions for a reasonable intake of calcium and phosphorus which leads to a ratio of calcium to phosphorus of 1 : 1.94 are however generally accepted, but there is no evidence as to what is the optimal ratio. At any rate, it would appear that if the calcium in the diet is adequate, the phosphorus will be adequate too. Milk, cheese and fish (especially small fish, in which the bones are also consumed), which are taken for their calcium, have a high phosphorus content as well.

It was observed that mottling of teeth of the rats could not be prevented by diet irrespective of the composition of the experimental diets, although a rich diet, such as the one including whole milk powder, considerably influenced and alleviated these symptoms also. A reduction of concentration of fluorine and an improvement of the diets of the animals gradually produced a marked beneficial effect on the mottled condition of their teeth as well. In the light of these and other observations, more especially that the incisors of the rat completely renew themselves every 30 days, the complete disappearance of the symptoms of mottling observed in the earlier experiments in which the animals were changed over to fluoride-free water may be explained.

It is suggested that the efficiency of whole milk powder may be tried on humans in areas of acute fluorine intoxication. The administration of bone powder in a suitable, assimilable form would also probably prove efficacious. Attempts are being made to prepare such a product from bone and to make it available for the use of all classes of people. The inclusion of liberal quantities of the small varieties of fish (the bones of which are invariably eaten) in the diet should also prove beneficial in the prevention and cure of fluorosis.

Fluorosis in farm animals may be controlled by supplementing their diets with bone meal.\*

The authors thank Professor V. Subrahmanyam for his valuable suggestions. Their thanks are also due to Dr. Y. N. Krishnamurthi, Radiologist in the Victoria Hospital, Bangalore, for his kind assistance in taking the x-ray photographs of the rats.

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(Concluded on opposite page)

\* When this paper was under preparation, it was privately learnt from Mr. T. J. Hurley, Director of Veterinary Services in Madras, that supplement of bone meal is proving highly beneficial to farm animals in areas where the disease is endemic.

# PLATE XI

## INFLUENCE OF MILK POWDER ON FLUORINE INTOXICATION IN RATS : S. C. PILLAI, R. RAJAGOPALAN & N. N. DE. PAGE 249.

X-ray photographs of rats from the series A (receiving normal diet, without sodium fluoride) and E (sodium fluoride but klim diet) showing control of fluorosis of bones as being due to inclusion of whole milk powder (klim) in the diets of the animals.

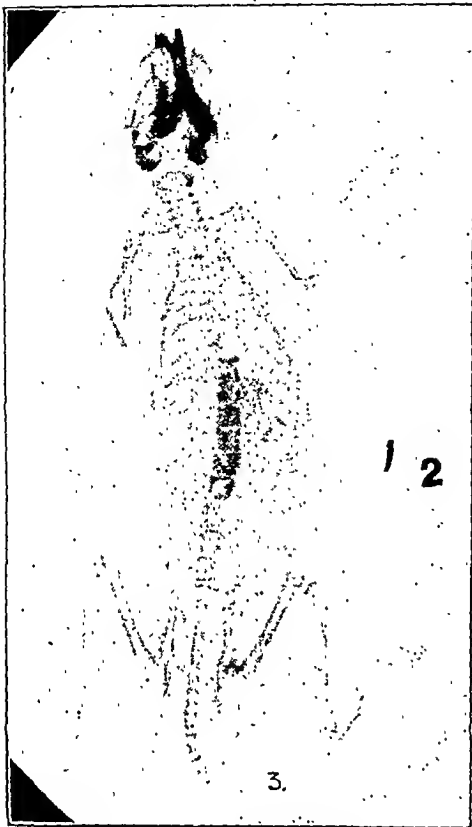


Fig. 3.—A rat on normal diet and tap water.



Fig. 4.—A rat similar to Fig. 3 but with supplement of bone powder.

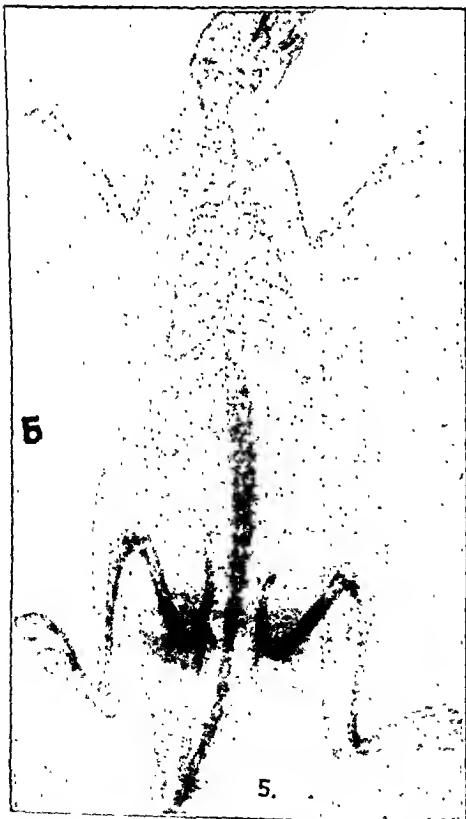


Fig. 5.—A rat from the E series (klim diet). Fluorine in water. No bone fluorosis.



Fig. 6.—A rat from the E series, which after 6 weeks received a supplement of bone powder for about a month.



Fig. 1. Case 1.—The left upper extremity is paralysed. There is œdema over the dorsum of the left hand.



Fig. 2. Case 1.—Showing the wasting of supraspinatus and infraspinatus muscles of the left side.



Fig. 3. Case 2.—Showing paralysis of the right upper extremity.



Fig. 4. Case 2.—Showing slight wasting of the right supraspinatus and infraspinatus muscles.

## REFINED LIVER EXTRACTS IN THE TREATMENT OF NUTRITIONAL MACROCYTIC ANÆMIAS

By S. K. SUNDARAM, B.A., M.D.

Madras Medical Service, Assistant in Medicine, Medical College, and Assistant to Physician, General Hospital, Madras

(From the Department of Medicine, Madras Medical College)

MINOT AND MURPHY's discovery of the value of liver in pernicious anæmia set in motion a universal attempt to extract from the liver its effective anti-pernicious anæmia principle. It is still evading isolation, and is still a hypothetical substance, hæmopoietin H, said to be formed in accordance with the law of mass action by the chemical interaction of two hypothetical substances, Castle's food or extrinsic factor, F, and the gastric or intrinsic factor, G. The nearest effective liver extract is the insoluble residue obtained by saturation with ammonium sulphate, and this is represented by anahæmin and similar extracts. Jacobson and Subbarow (1941) have reported that further purification splits the anti-pernicious anæmia principle.

Following the introduction of anahæmin, and its brilliant success in Addisonian pernicious anæmia, refined liver extracts were largely used in nutritional megalocytic (tropical macrocytic) anæmias. The results were generally disappointing. The inference appeared inevitable that the agent, effective against nutritional macrocytic anæmia, was different from the anti-pernicious-anæmia principle, and was lost in the process of refinement of liver extract.

This feeling, which is widespread, was given definite shape by Wills, Clutterbuck and Evans (1937), Wills and Evans (1938) and Napier (1938). Wills and Evans (1938) and Napier (1939) quite logically went further and suggested that the Castle's extrinsic factor had little or no relation to the causation of nutritional macrocytic anæmia.

Foy and Kondi (1939) in Macedonia were among the first to report good response to anahæmin in nutritional macrocytic anæmia. They were cautious in their conclusions. They wondered if nutritional macrocytic anæmia in Macedonia was different in origin from its counterpart in India. Napier (Napier and Neal Edwards, 1942) found cure in some cases of

tropical macrocytic anæmia with massive doses of anahæmin, but preferred to believe that the good hospital diet, which his patients had, might have been principally responsible for the cure. Fairley (1940) also found anahæmin effective. Trowell (1943) has had good results with 8 to 15 c.cm. weekly of campolon, 16 c.cm. weekly of hepatex T and 12 c.cm. weekly of anahæmin. He does not give his total dosage.

Some of us in the Madras General Hospital had also noticed that concentrated liver extracts very often produced little or no reticulocyte response, which was then the *sine qua non* of therapeutic potency. I had found that nevertheless there was an occasional restoration of red cell count to normal or nearly normal level. I was not then aware of Murphy's (1933) earlier similar findings and his recommendation 'to rely more on increases in the erythrocytes as a means of determining the actual comparative effectiveness of the various substances (liver extracts) used'. Puzzled by our want of quick results, we readily accepted the prevailing view of the inefficacy of refined liver extracts in nutritional macrocytic anæmia.

It was with this background that from August 1940 I was afforded facilities to investigate the effect of refined liver extracts in cases of nutritional macrocytic anæmia admitted to Colonel McRobert's wards in the Government General Hospital, Madras. We were beginning to wonder whether we should not have waited a little longer for results in our earlier cases. We then gathered that the impression was gaining ground among American hæmatologists that the full hæmopoietic effect of liver extracts may last for six to eight weeks. We decided to allow a similar period in our investigations. Our results in fifteen cases of nutritional macrocytic anæmia with and without diarrhoea are given in the appended table.

All the patients were uniformly placed on a basic diet consisting of one and a half pints of milk, two ounces of brown sugar, two pints of coffee containing per pint three ounces of milk and an ounce of sugar, six ounces of white bread, one ounce of butter, one ounce of arrowroot, biscuits, two eggs and an orange. To this were generally added two ounces of idlis (a steamed rice and gram preparation), four to eight ounces of table rice, half to one pint of curd, and sometimes four ounces of mutton or fish curry.

It may be contended that this diet might be the chief factor responsible for cure in our cases, even as the good diet was supposed to be by Napier in his. But in none of our cases was there any rise in reticulocytes or red cells or hæmoglobin till liver extract was started. In two of them, iron was given by mistake for a long time in addition to this diet, without any hæmopoietic response.

The refined liver extracts tried were largely anahæmin (B.D.H.), examen (Glaxo) and reticulogen (Lilly). Twelve c.cm. of the liver extract were given intramuscularly for each patient,

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2 c.cm. per injection on alternate days. (In only two early cases we unnecessarily used a second liver extract to see if there would be a secondary reticulocyte response.) Our dosage is not massive. It is found to correspond with Dyke's (Della Vida and Dyke, 1942) recommendation of 10 c.cm. in two weeks as a standard dosage of parenteral preparations of liver for the initiation of treatment.

The results with refined liver extract in our cases of nutritional macrocytic anæmia were uniformly gratifying. In only two cases (2 and 14) out of fifteen listed here, we failed to secure full hæmopoietic response. In one of them (case 2) we failed too, with subsequent crude liver extract and with blood transfusion. In both there were septic or infestative inhibiting factors preventing a full hæmopoietic response to specific replacement therapy.

In one patient (case 5) we produced complete remission in a relapse with marmite alone. Marmite was ineffective in patient 14 who had diarrhoea.

I wish to draw special attention to the effect of anahæmin on the gastro-intestinal manifestations of nutritional macrocytic anæmias. It was our aim at the beginning to try refined liver extracts only in simple uncomplicated nutritional macrocytic anæmia; but in the course of our investigations I had a good chance of noting the effect on cases of nutritional macrocytic anæmia with diarrhoea, sometimes sprue-like. Castle *et al.* (1935) noticed in Porto Rico that parenteral liver extract containing fraction G of Cohn, unaided by dietetic control, produced complete lingual and gastro-intestinal as well as hæmopoietic remission in sprue. It was a revelation to me that a refined liver extract, such as anahæmin, devoid of all the soluble factors of liver extract on saturation with ammonium sulphate, could be equally effective in curing the glossitis and diarrhoea, fatty or not, as well as the anæmia of nutritional macrocytic anæmia. But so it was. In patients 1, 6, 7, 9 and 10 we obtained complete gastro-intestinal remission without restriction of diet. In patient 13 we failed to obtain such a remission with mere dietetic control and hydrochloric acid, but with anahæmin we obtained remarkably quick results in all his manifestations. In a relapse of this patient's symptoms, nicotinic acid and hydrochloric acid were successful in controlling the glosso-intestinal manifestations. Patient 14 did not show complete hæmopoietic remission because of his septic complications, but anahæmin enabled him to do away with dietetic restriction to control his diarrhoea.

Patients 13 and 14 had a primary trial with Teddington liver extract TCF of which a generous sample was placed at our disposal by the manufacturers. In both of them this brand of liver extract failed. Anahæmin given after six weeks had a very striking curative effect, especially in case 13; case 14 had a septic complication. TCF extract also failed in a straight-

forward case of uncomplicated macrocytic anæmia, not included in this series, because he left Madras before the effect of anahæmin could be gauged. (Subsequent trials of TCF extract in massive dosage have been more satisfactory; results were seen even in a case with marked neurological involvement. These cases are not included in this report for want of complete investigation and follow-up after the first few months of 1942.)

One can very well understand the quicker results of crude liver extracts in nutritional macrocytic anæmia. Nutritional defects are generally multiple, and crude liver extracts meet a wider defect and, moreover, produce a sense of well-being too. This action explains but does not justify their indiscriminate use in practice. There is no doubt that, in uncomplicated nutritional macrocytic anæmia, marmite, as a very rich source of Castle's extrinsic factor, is quite as good in the long run as the most potent liver extract which supplies the active anti-anæmic factor. It is now generally admitted, however, that parenteral administration of liver extract offers the best method of treatment because of its depot action. My observation on fifteen cases covering August 1940 to April 1942 (the first ten cases by May 1941) shows that refinement of liver extract to the anahæmin stage does not interfere with its potency against nutritional macrocytic anæmia. It seems too that such refinement does not destroy whatever curative effect crude liver extract may have on the gastro-intestinal manifestations of complicated nutritional macrocytic anæmia. Further experience has only served to strengthen my original conclusions arrived at in 1941.

I am only too conscious of the gross imperfection of the hæmatological technique and counts in this report. Whatever shortcomings there are, are uniform and do not vitiate the basis of my contention of the efficacy of refined liver extracts in nutritional macrocytic anæmias, with or without diarrhoea. Bone-marrow studies are being made increasingly difficult with a growing multiplicity of expert views and nomenclature. It is my belief, born of arm-chair studies of some of these expert observations rather than of competent personal study, that the morphology of the marrow and of peripheral blood offers very poor help in differential diagnosis of the different macrocytic anæmias. Pernicious anæmia has to be differentiated from other macrocytic anæmias, chiefly by its other associated defects, such as acid-producing, leucopoietic, thrombopoietic, neuopoietic and so on. Its bone-marrow picture is, however, one of pure defect of hæmopoietin, whereas the picture in macrocytic anæmia arising from faulty nutrition, absorption, storage or utilization (from inhibition) is a mixed one due to multiplicity of defect.

#### *Three typical case reports*

*Case 5.*—A Hindu male, 40 years old, admitted on 15th December, 1940, with 1.2 mil. red cells per c.mm.,

APPENDIX  
Laboratory data

BEFORE TREATMENT																	AFTER TREATMENT			
Case number	Red cells in mil. per c.mm.	Hb % (Zeiss)	C.I.	V.I.	Reticulo-cytes %	W.B.C. in thousands	Differential white cell count %					Thrombo-cytes in thousands	Sternal marrow	Serum proteins %	van den Bergh	Kahn test	B.P. in mm. Hg.	Maximal		
							N.	E.	B.	M.	L.							Reti-culo-cytes %	Red cell count	Hb %
1	1.6	40	1.25	1.04	0.5	4.0	60	2	..	3	35	122	Meg.	5.2	Neg.	Twice doubtful.	94/54	18	4.63	98
2	1.1	32	1.46	1.32	0.5	3.4	58	3	..	5	34	..	Do.	4.4	Do.	Neg.	126/70	16	3.9	80
3	0.8	25	1.5	1.2	0.4	5.0	77	..	..	..	23	..	Do. (mild). No M.P.	5.1	Ind. faint positive.	Do.	..	35	5.1	110
Re-admitted. 4	2.84	65	1.13	1.02	2.2	4.0	..	..	..	..	..	..	Meg. marked.	5.0	Ind. + ve. 5 units.	Do.	120/85	22	3.6	80
	1.2	33	1.4	1.1	Less than 1%	5.0	..	..	..	..	..	..	Do.	4.8	Ind. faint positive.	Do.	90/40	8	5.2	105
5	1.2	40	1.7	1.5	Do.	4.8	58	3	..	3	36	..	Moderate meg. Meg. marked.	5.4	Do.	Do.	105/50	8	5.1	102
6	1.5	40	1.3	1.7	1.4	5.2	61	..	2	4	33	..	..	4.8	Do.	Do.	76/52	14	5.1	100
7	1.75	50	1.4	1.4	0.9	6.8	72	4	..	..	24	..	Do.	4.1	Do.	Do.	75/40	9	4.22	88
8	2.5	65	1.3	..	1.5	6.9	65	3	..	2	30	..	Do.	4.4	Do.	Do.	84/50	10	5.2	105
9	2.5	65	1.3	1.3	1.5	5.0	52	2	..	..	46	..	Do.	4.8	Neg.	Do.	92/60	7	4.0	90
10	1.6	35	1.1	1.4	3.0	6.0	58	..	..	..	42	..	Do.	4.8	Ind. faint positive.	Do.	110/75	12	5.0	100
11	1.65	50	1.5	0.99	1.0	3.8	58	1	1	..	40	..	Moderately meg.	3.8	Delayed direct, faint + ve.	Do.	120/85	5	4.4	90
																			5.0	100
12	1.7	40	1.1	1.26	1.6	7.2	54	2	..	2	42	..	Meg. marked.	5.0	Biphasic 4.2 units.	Do.	115/70	8	4.35	90
13	2.16	72	1.7	1.3	0.1	..	..	..	..	..	..	230	Meg.	5.2	Ind. faint + ve.	Do.	..	3	3.3	98
14	2.85	60	1.1	0.7	1.0	6.0	..	..	..	..	..	..	Do.	5.5	Direct neg.	Do.	110/70	4	3.6	82
15	1.6	42	1.3	1.14	1.2	6.2	..	..	..	..	..	..	Do.	5.3	Ind. + ve faint.	Do.	..	12	3.62	74
																			3.2	60

Legend of the symbols used.

C.I. = Colour index.  
V.I. = Volume index.  
N. = Neutrophils.  
E. = Eosinophils.  
B. = Basophils.

M. = Monocytes.  
L. = Lymphocytes.  
B.P. = Blood pressure.  
Meg. = Megaloblastic.  
Ind. = Indirect.

40 per cent hæmoglobin (Zeiss), V.I. 1.5, megaloblastic sternal marrow and less than 1 per cent reticulocytes; discharged on 29th January, 1941, with 5.1 mil. red cells and 102 per cent hæmoglobin after 6 c.cm. of reticulogen. Maximal reticulocytic response 8 per cent. Re-admitted on 27th August, 1941, with 2.6 mil. red cells and 70 per cent hæmoglobin. Two ounces daily of marmite from 3rd September, 1941, to 7th October, 1941, raised his red cell count to 4.8 mil. and hæmoglobin to 100 per cent by 7th October, 1941. Maximal reticulocyte response was 6 per cent. This patient gave no history of diarrhoea or of paræsthesiæ. He had free hydrochloric acid in his stomach juice.

Case 6.—A Hindu male, 25 years old, admitted on 19th December, 1940, with large, pale, frothy diarrhoea with very high total fat and free fatty acid content. Twelve c.cm. of anahæmin without restriction of diet raised his red cell count and hæmoglobin from 1.5 mil. per c.mm. and 40 per cent to 5.1 mil. and 100 per cent respectively. His V.I. on admission was 1.7 and sternal marrow showed a well-marked megaloblastic reaction. Maximal reticulocyte response was 14 per cent. Gastric juice contained free hydrochloric acid.

Case 8.—A Hindu male, 37 years old, admitted on 14th November, 1940, with foul, frothy and fatty (total and soaped fat and free fatty acid high) diarrhoea of six months, histamine-fast achlorhydria and well-marked megaloblastic marrow. Twelve c.cm. of anahæmin raised his red cell count from an initial 2.5 mil. per c.cm. to 5.2 mil. and hæmoglobin from 65 to 105 per cent on 29th January, 1941. Maximal reticulocyte response was 10 per cent.

#### Summary

Fifteen cases of nutritional macrocytic anæmia with and without diarrhoea are reported as having well responded to refined liver extracts of the anahæmin type.

It is therefore inferred that refinement of liver extract by saturation with ammonium sulphate does not affect its potency against nutritional macrocytic anæmia.

The mechanism of production of nutritional macrocytic anæmia may be by deprivation of hæmopoietin to the bone marrow by defective supply of Castle's food factor even as the genesis of pernicious anæmia is supposed to be by similar deprivation by defective secretion of Castle's gastric factor. There is no case for postulating a totally different mechanism for the two anæmias.

Practically all the hæmatological studies on the cases reported here were made by Lieut.-Colonel G. R. McRobert's senior house physicians at the time, by Dr. P. Ramachander in the earlier cases and Dr. V. S. Raghunathan in the later ones. The volume index and thrombocyte count determinations were made by the clinical pathologist of the hospital at the time. The biochemical investigations were made by the department of biochemistry of the Madras Medical College. I am grateful to them for their help. My indebtedness to Lieut.-Colonel G. R. McRobert, I.M.S., Professor of Medicine, Medical College, and Physician and Superintendent, General Hospital, Madras, for his constant drive and encouragement and helpful discussions cannot find adequate expression.

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## TREATMENT OF BLACKWATER FEVER

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CAPTAIN, I.M.S.

*Ætiology.*—Thirty-seven cases of blackwater fever are recorded. The condition was precipitated during the administration of quinine (18 cases), pamaquine (18 cases) and mepacrine (1 case).

In all cases there was history of malaria, one to five attacks during the twelve months preceding the attack of blackwater fever. Thirty-four cases were treated for malignant tertian malaria, and the remaining three cases for benign tertian malaria. In the latter three cases, during the particular bout of fever which was clinically benign tertian, malignant tertian rings were not demonstrated in the blood by careful examinations, but in two of them previous infection with

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#### Later communication

(a) Since sending the main article for publication, I have had a chance of studying two patients with sprue syndrome (diagnosis based on history, fat content of stools, flat glucose tolerance curve) with normoblastic bone marrow on admission. After failure of TCF liver extract and hydrochloric acid in full doses, in one of nicotinic acid, in the other of riboflavin, anahæmin produced striking and immediate lingual and gastrointestinal remissions.

(b) Specific therapy in Addisonian pernicious anæmia is known to induce a reversion from megaloblastic to normoblastic marrow in 24 hours. I have recently studied in two cases the effect of anahæmin on the marrow of nutritional macrocytic anæmia. Two microphotograph prints of sternal marrow smear are annexed, one made before and the other in 20 hours after the first 4 c.cm. of anahæmin given to a patient with nutritional macrocytic anæmia (see plate XIII, figures 1 and 2). I am grateful to Dr. D. Govinda Reddy, Professor of Pathology, Madras Medical College, for them. They speak for themselves of the striking reversion to the normoblastic condition in under one day. Davidson et al. (1942: Quart. J. Med., 11, 19) have reported the commencement of such reversion in 6 hours in pernicious anæmia. They argue that such early reversion demonstrates easy convertibility of a megaloblast into a normoblast. It is out of place here to discuss fully the implications of this observation.

malignant tertian malaria was proved by the presence of characteristic gametocytes in the blood.

None of the patients were actually febrile with a malarial bout of fever. They were up and about taking antimalarial drugs and doing various grades of work, with the exception of one who was bed-ridden and three who were on a train journey.

Thirteen of the patients had been taking quinine as a prophylactic, and the rest were on treatment with the antimalarial drugs.

All the cases were recorded between October and March, with the exception of one in April.

Thirty-five of the patients were weak and debilitated, while two appeared to be in good health.

One had a positive W.R., and had taken one course of anti-syphilitic treatment.

Hæmolytic substances were demonstrated in the peripheral blood of three patients. Their presence was very transitory; they were found in samples of blood taken five minutes before other samples which showed early hæmoglobinæmia, but not in the samples taken ten minutes before that. In one of these patients who seemed to show three distinct attacks of hæmolysis within the next fifteen minutes, hæmolytic substances were demonstrated in two samples, 1 and 4, out of six samples of blood taken every two minutes during that period.

This probably indicates that during a clinically single attack of hæmolysis, hæmolytic substances are poured out in distinct gushes, and become almost immediately fixed to the red blood cells; in the above cases it must have been within five minutes. To get the hæmolytic serum, the red blood cells had to be centrifugalized off within two minutes, as after that it lost its hæmolytic properties, although hæmolysis continued in the test tube.

It was further observed that the serum had the following properties: 1. It hæmolyzed infected and non-infected red cells. It could not be proved that infected cells were more susceptible to hæmolysis. 2. Traces of quinine, 1 in 3,000, pamaquine, 1 in 10,000, and mepacrine, 1 in 500, accentuated the hæmolytic process; this proved that mepacrine could produce blackwater fever, but it does not do so often, because it required larger concentrations of it to help the process. 3. The hæmolytic process was prevented by the addition of antivenene, 1 in 300. Clinically a recurrence of hæmolysis did not occur after ninety-six hours in any of the control cases.

*Treatment.*—Antivenene was used to prevent recurrence of intravascular hæmolysis with absolute and definite results. Using 20 c.cm. of the concentrated serum intravenously at once, and repeating 10 c.cm. every four hours for the next seventy-two to ninety-six hours, it was found that a second attack of hæmolysis did not occur. Using three controls with a smaller dosage, the hæmolysis was found to be milder,

and the patients were, as it were, allowed to have one to four attacks of hæmolysis, the maximum number recorded by changes in the colour of the urine being five.

The prevention of precipitation of acid hæmatin in the kidney tubules was ensured by taking the following precautions: by keeping the urine strongly alkaline throughout the twenty-four hours; by withholding the sodium chloride till the urine was alkaline; by not allowing the temperature of the patient to rise higher than 102°F.

Immediate alkalization of the urine was acquired by giving 150 c.cm. of a 4 per cent sodium citrate solution intravenously, followed by one dram doses of sodium citrate two to four-hourly by mouth. Where vomiting did not allow the result to be achieved, a total of six to eight drams of sodium citrate could be infused intravenously by drip in twenty-four hours.

To ensure diuresis, glucose solution 25 per cent, 100 to 200 c.cm. with vitamin C, 100 to 200 mg. was given intravenously every four hours. Glucose saline was withheld during the early stages when the urine was acid, for the reasons given above. In cases with threatening anuria, sodium sulphate, 4.285 per cent, was an useful adjunct to glucose and vitamin C. Glucose also supported the circulation, and vitamin B 25 mg. in twenty-four hours was added.

Vomiting was checked by sodium citrate given by the mouth, and could be further relieved by an injection of atropine gr. 1/100 to 1/50 given intravenously. Vomiting usually disappeared twenty-four hours after an attack of hæmolysis, and was apparently caused by the irritation of the bile in the stomach (to distinguish it from the vomiting of later stages which may develop from kidney or liver failure). An automatic stomach-wash, produced by giving the patient a pint or more of a 2 per cent sodium bicarbonate solution and subsequent vomiting, gave immense relief in other cases. Calcium gluconate, 20 c.cm. of a 10 per cent solution, repeated if necessary in two to four hours, checked the vomiting in cases showing renal acidosis or alkalosis produced by severe vomiting, conditions in which there is a fall in the blood calcium. A very useful drink retained by many patients was made as follows: glucose dr. 2, sodi bicarb. dr. 1, and lemonade one bottle, given iced.

Blood transfusion was used in three cases in which hæmoglobin had fallen to 20 per cent. Reactions were prevented by the following precautions: by matching the blood under the high power of the microscope; by using 120 c.cm. of a freshly prepared 4 per cent sodium citrate solution for each 400 c.cm. of blood; by collecting the blood freely at room temperature; by not shaking the blood and the citrate to ensure admixture as this is unnecessary; by using no warming apparatus before infusing the blood which was to be given at room temperature; by ensuring that the urine was alkaline. This latter

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## NOTE ON THE TREATMENT OF ANGULAR CONJUNCTIVITIS WITH RIBOFLAVIN

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THE successful treatment by riboflavin of a number of cases of superficial keratitis was described in two previous papers (Aykroyd and Verma, 1942; Verma, 1942). In the course of this work it was observed that a number of

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precaution was also important because the infused blood was equally liable to hæmolysis.

Blood was still positive for malignant tertian malaria in seventeen cases after the hæmolysis. No antimalarial drugs were used. A low-grade pyrexia persisted in thirty-one cases from three to twelve days, but probably it was due to the same causes as the fever in anæmia, as it was still present when the serum showed no evidence of hæmoglobinæmia. However it would appear that antimalarial drugs could be used if antivenene was given at the same time, but this was not tried in any of the cases.

Secondary anæmia was treated with fersolate, vitamin B, vitamin C, and sometimes by the use of crude liver extracts given by injection if the response to the other drugs was not adequate. Cod-liver oil was given to all debilitated cases, and a generous diet containing chicken, fish, eggs, fruit, milk and vegetables was given from the very start, as soon as the vomiting stopped. Convalescence was rapid.

**Result.**—Thirty-six cases were treated with antivenene, and all recovered. One case not treated with antivenene, as it was not available, died in spite of all other measures after three attacks of hæmolysis. No kidney or liver complications were recorded in any of the thirty-six cases. No stimulants were used. Oxygen was given to very anæmic cases, and the circulation was supported by glucose till blood transfusion was given. No antimalarial drugs were given to any of the cases after the attack of hæmolysis was over, although some of them still showed parasites.

**Conclusions.**—1. Hæmolytic substances are responsible for an attack of blackwater fever. Their presence is transitory and therefore difficult of demonstration, but by well-timed examination they can be demonstrated.

2. Antimalarial drugs accentuate the hæmolytic process. Mepacrine does so only in greater concentration, and hence blackwater fever seldom occurs with mepacrine.

3. Antivenene neutralizes the effect of hæmolytic substances in blackwater fever, and so is very useful in preventing further hæmolysis. Its use during the administration of antimalarial drugs to blackwater fever cases has however not been tried.

patients with superficial keratitis, associated with angular stomatitis and other signs of riboflavin deficiency, were also suffering from angular conjunctivitis, and that the latter condition tended to clear up on the administration of riboflavin. Further investigations on the effect of riboflavin therapy in cases showing angular conjunctivitis were then undertaken. These investigations were interrupted by Army service, and since it will probably be some time before the work can be resumed, the preliminary observations are here recorded.

**Angular conjunctivitis and the Morax-Axenfeld bacillus.**—This diplo-bacillus was described in 1896 by Morax and Axenfeld simultaneously (Duke-Elder, 1938). It is found in abundance in smears from cases of angular conjunctivitis. It is a saprophyte and is said to produce conjunctivitis by excreting an exogenous protein-dissolving ferment, which acts by macerating the epithelium. The specific treatment of angular conjunctivitis associated with this bacillus is by drops of zinc sulphate solution, which banishes the symptoms rapidly. The action of zinc, according to Duke-Elder (*loc. cit.*), is not a bactericidal one, for the diplo-bacillus grows well in a culture-medium containing zinc; the zinc acts by inhibiting the proteolytic ferment secreted by the bacillus and so rendering it impotent.

**Effect of riboflavin therapy.**—Smears from cases of angular conjunctivitis associated with signs of riboflavin deficiency showed abundant Morax-Axenfeld bacilli (MAB). On treatment by the administration of riboflavin, the angular conjunctivitis disappeared and the smears became negative. No local treatment was given. Twenty cases were treated, 12 males and 8 females. Of these, 2 showed superficial keratitis and 14 had other signs of riboflavin deficiency, i.e. angular stomatitis and sore and fissured tongue. Some of the male patients showed an eczematous condition of the skin of the scrotum, characteristic of riboflavin deficiency. In only 3 cases was angular conjunctivitis present without other signs of riboflavin deficiency. Some typical cases are described below :—

(1) F. 30. Complained of photophobia, itching, burning, watering and discharge from the eyes for a period of 6 weeks. Examination showed angular conjunctivitis and superficial keratitis. Conjunctival smears were highly positive for MAB. Three mgm. of riboflavin were given by intramuscular injection daily for 7 days. All symptoms and signs disappeared, and the conjunctival smear became negative.

(2) F. 11. This patient complained of pain, watering and itching in both eyes for 10 months. She had xerosis conjunctivæ, angular conjunctivitis, corneal 'stippling', angular stomatitis and fissured tongue. The conjunctival smear was positive for MAB. After the intramuscular injection of 4 mgm. of riboflavin daily for 5 days the eye symptoms and signs cleared up, and the smear became negative.

(3) F. 30. Had angular conjunctivitis, superficial keratitis and angular stomatitis. Duration over 3 weeks. Treatment with riboflavin, 5 mgm. daily for 8 days by mouth, was followed by relief of eye signs

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## BERBERINE IN MALARIA\*

## A PRELIMINARY NOTE

By SIR UPENDRANATH BRAHMACHARI, M.A.,  
M.D., Ph.D.Professor of Tropical Medicine, Carmichael Medical  
College, CalcuttaCHOPRA (1933) has pointed out that berberine,  
the active principle of berberine-containing

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with disappearance of MAB, previously present, from  
the smear.

(4) M. 26. Complained of itching, burning, watering  
and photophobia in both eyes. Stated that he had  
suffered from recurring attacks for 3 years, in the  
winter months. This patient had blepharitis, angular  
conjunctivitis, angular stomatitis and fissured tongue,  
and the skin of the scrotum was itchy, rough and scaly.  
The conjunctival smear showed numerous Morax-  
Axenfeld bacilli. He was treated by injection of ribo-  
flavin, 4 mgm. daily intramuscularly for 11 days. The  
ocular signs and symptoms disappeared, and the smear  
became negative. Simultaneously the scrotal skin  
became smooth and the angular stomatitis disappeared.

(5) M. 24. Complained of burning, itching and  
watering in the eyes for 3 months. Angular conjunc-  
tivitis and well-marked angular stomatitis were present.  
The conjunctival smear was highly positive for MAB,  
the organism being separated in pure culture. After  
7 days' treatment with riboflavin (3 mgm. intramus-  
cularly each day) the eye signs and symptoms dis-  
appeared, and no bacilli could be found in the smears.

(6) M. 43. In this case angular conjunctivitis had  
recurred after a month of treatment with zinc. No  
signs of riboflavin deficiency were present. The con-  
junctival smear was highly positive for MAB, and  
the organism was grown in pure culture. Treatment  
consisted of 40 mgm. of riboflavin given orally and  
5 mgm. daily by intramuscular injection over a period  
of 3 weeks. The angular conjunctivitis disappeared,  
and the smear became negative.

In a series of bacteriological experiments  
preliminary evidence was obtained that ribo-  
flavin has an inhibitory effect on the growth of  
the Morax-Axenfeld bacillus *in vitro*. Further  
work is, however, necessary for conclusive results.

Angular conjunctivitis associated with the  
presence of the Morax-Axenfeld bacillus appears  
to be a common condition in many countries.  
Whether riboflavin therapy is of value in cases  
showing no obvious evidence of riboflavin  
deficiency requires further investigation. In the  
great majority of cases observed in this series  
signs of riboflavin deficiency were present.

## Summary

Cases of angular conjunctivitis were success-  
fully treated by the administration of riboflavin.  
Before treatment, smears showed numerous  
Morax-Axenfeld bacilli which disappeared after  
treatment. In the majority of cases, ocular and  
other signs of riboflavin deficiency were present.

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\*The Editor publishes this preliminary note by this  
eminent worker, but is rather sceptical, and would like  
sound clinical observations in confirmation.—EDITOR,  
I. M. G.

plants, has some remarkable properties in its  
behaviour towards the parasites of malaria.  
Its sulphate has been found to liberate the  
parasites into the peripheral circulation from the  
internal organs, so that, whereas blood films  
taken before the administration of berberine are  
negative, those taken after it become positive.  
Sabatini (1928) used it as a provocative agent  
in the diagnosis of latent malaria. Its action  
resembles what Chopra and Das Gupta (1928)  
observed in the case of pentavalent organic  
antimonials which when injected intravenously  
have the remarkable properties of expelling  
*Leishmania donovani* from the internal organs  
to the peripheral circulation. Perez André  
(1927) advocated berberine in the treatment of  
malarial splenomegaly.

This property of berberine was, however, not  
taken advantage of in the treatment of malaria  
acting, as it does, as a powerful agent in helping  
quinine to attack the parasites. Quinine has  
the property of driving malarial parasites into  
the internal organs, and for some time after  
its administration no parasite may be found in  
the peripheral blood; this may give a false  
impression that the patients have been parasite  
free. As a result of the disappearance of the  
parasites from the peripheral blood there is waste  
of quinine, as it is quickly excreted after adminis-  
tration. Further it takes a longer time to come  
in contact with the parasites when they have  
shifted to the internal organs than when they are  
present in the peripheral blood. The same  
also happens when they are not present in the  
peripheral circulation as in cases of chronic  
malaria. Here berberine may step in and help  
in many ways:—

(a) It liberates the parasites from the internal  
organs and brings them in close contact with  
quinine in the peripheral circulation.

(b) As a result of this, there is no loss of time  
in the action of quinine on the parasite, which is  
likely to take place when they are away from  
the peripheral circulation.

Berberine sulphate is a safe drug and can be  
used with impunity intravenously. Its toxicity  
is rather low. It may be mentioned here that  
Das Gupta and Dikshit (1929) have shown that  
berberine is toxic to *Leishmania tropica* in a  
concentration as low as 1 in 80,000, while power-  
ful protoplasmic drugs such as quinine require  
about 80 times the concentration to produce the  
same effect.

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## PFEIFFER BACILLUS MENINGITIS

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and

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MENINGITIS caused by *Hæmophilus influenza* (Pfeiffer's bacillus) is of infrequent occurrence not only in our country but all over the world. Huntington and Wilkes-Weiss (1936) found only 54 cases which were admitted into the St. Louis Children Hospital during a long period of 18 years from 1918 to 1935. During the same period, however, there were 160 cases of meningococcal meningitis, 74 of streptococcal meningitis, 62 of pneumococcal meningitis and 22 of staphylococcal meningitis. Neal, Jackson and Appelbaum (1934) recorded 111 cases during a period of 22 years. Jones (1937) after reviewing all the records of the St. Thomas's Hospital, London, for 15 years found only 6 cases. Indian literature on the subject is very poor. Elias and De (1942) reported only 4 cases which they could collect from the records of the Medical College Hospitals, Calcutta, during a period of 6 years and 10 months from 1935 to November 1941.

In the past, this disease was known as influenzal meningitis, but with the newer conception of the etiology of influenza, the old nomenclature has been replaced by the term Pfeiffer bacillus meningitis. It is true that the virus of influenza may affect the nervous system and produce clinical manifestations of meningo-encephalitis, but it is not known to give rise to a true inflammatory reaction in the leptomeninges, nor to produce a purulent cerebrospinal fluid. In such cases the latter remains perfectly clear and sterile. It will thus be seen that this variety of meningitis does not occur as a complication of clinical influenza, nor is it caused by the virus of influenza. It is essentially due to an infection of the meninges by the pus-forming organism, *Hæmophilus influenza*.

This variety of meningitis is primarily a disease of infancy and early childhood, more than 88 per cent of cases occurring in children within one year (Roy and Steiner). In the series reported by Elias and De (1942), all the 4 cases occurred during the first year of life, the ages being 6, 8, 8, and 9 months respectively. In the case recorded below, the age was only 3 months. Very occasionally, however, one may come across an adult suffering from the disease. It is not definitely known why the disease is usually found in small children. Perhaps the defensive mechanisms are not sufficiently developed in early childhood. This idea is also supported by the fact that the mortality from Pfeiffer bacillus meningitis is not high when the disease affects adults.

The mode of infection and pathogenesis of Pfeiffer bacillus meningitis are, in general, similar to those in other forms of meningitis.

*Hæmophilus influenza* may have its normal habitat in the nose, naso-pharynx and the air sinuses. Like the pneumococci and other bacteria residing in the nose and throat, these organisms may be conveyed by droplet method during acts of talking, sneezing and coughing, into the nose and throat of an otherwise healthy person. This is very important in the case of parents, either one or both of whom may harbour the organisms in the naso-pharynx without suffering from any disease and therefore be capable of transmitting them to their offspring. A very interesting case of Pfeiffer bacillus meningitis was recorded by Schmidt and Weinberg (1924) in an infant aged 11 months, following a trauma on the head as the result of a fall; the Pfeiffer's bacillus was isolated 7 times in succession in pure culture from the cerebrospinal fluid as well as from the throat and nose. Both the parents were carriers of *Hæmophilus* infection, the father harbouring the organisms in his nose and the mother in her throat. After these bacteria have gained entrance into the nose and throat, the question of infection of the meninges is a matter of time and opportunity. It is, however, essential that the resistance of the mucous membrane which normally serves as a protection against bacterial infection must undergo deterioration by catarrhal inflammation before the *Hæmophilus influenza* can initiate its pathogenic effects. An attack of cold, sinusitis, middle ear inflammation or some such morbid condition usually precedes the meningeal involvement. In such circumstances, when once the barrier of resistance is overcome, the organisms reach the meninges either directly through the veins and lymphatics or *via* the blood stream. Personally, the writers support the latter idea, as on many occasions the senior writer was able to isolate the organisms from the blood during life. In one case, proved to be Pfeiffer bacillus meningitis, blood culture showed the causative organisms, and, after death, pus from the frontal and maxillary sinuses revealed *Hæmophilus influenza* in large number. Similar observations were made by others. Neal *et al.* (1934) did blood culture in 8 of their cases and obtained positive results in 7. They also state that in some of their cases, though organisms failed to grow in blood culture, they noticed clinically all the features of a generalized infection, 5 patients having a hæmorrhagic rash and 3 joint involvement. In one of these cases, *Hæmophilus influenza* was also isolated from the purulent fluid aspirated from the joint cavity. Rivers and Kohn (1921) carried out blood culture in 18 cases suffering from Pfeiffer bacillus meningitis and obtained positive results in 8 of them. Hart (1932) obtained positive results in 4 out of 7 of his cases.

After they reach the blood stream, the organisms localize in the meninges and induce an acute inflammatory reaction. The serous membranes become intensely congested and covered with a frankly purulent exudate. The

picture at this stage is indistinguishable from that of any other type of meningitis. The cerebrospinal fluid tension is considerably raised, and this fact dominates the clinical picture leading to unconsciousness; tremors and convulsions. There is no individual symptom or group of symptoms by which one can arrive at a definite diagnosis. The clue to the nature of the infection is usually obtained by examining the cerebrospinal fluid microscopically and also bacteriologically. The disease has usually a fatal termination, very few recoveries having been reported. Rivers (1922) reported 100 per cent mortality in 32 cases. Bloom (1931) collected 302 cases with a mortality of 92 per cent. Hart (1932) found 32 cases with 2 recoveries. Neal *et al.* (1934) found only 4 cures in a series of 111 cases. The prognosis is, however, more hopeful in adults and older children, and a few cases of recovery have been reported by Gibbens (1931) and Appelbaum (1935). We have not seen any recovery in the cases admitted into the Medical College Hospitals.

Treatment of Pfeiffer bacillus meningitis is almost hopeless. Repeated lumbar puncture, injection of colossal silver and anti-serum in heroic doses have all been tried by different observers but nothing has so far influenced the gloomy nature of the prognosis. In recent times, sulphonamides either alone or in conjunction with anti-serum have been used; reports are conflicting. The drug of choice has been sulphapyridine, which has been administered in very high doses, a baby of 10 months being given as much as 24 to 30 grammes of the drug. No definite conclusion in favour of or against the drug is yet justifiable.

In view of the scarcity of the report of these cases in this country, we put on record another case in addition to the four already reported. The condition does not seem to be very uncommon, and more cases are likely to be diagnosed, if looked for, in the acute illness of infancy or childhood showing signs of meningeal irritation.

#### Case note

A baby, aged 3 months, was admitted on 11th September, 1943, for fever and unconsciousness. On enquiry, it was revealed that fever started with severe cold. The child had been unconscious for the last 24 hours.

On examination.—The child was somewhat emaciated and looked dehydrated. He was unconscious and restless. Cyanosis was present in the fingers and toes. Temperature—102°F. Pulse—180. Respiration—56. The tongue was coated and dry. There was no patch in the tonsils. The lungs showed scattered râles and rhonchi. The heart showed embryocardia. The spleen was palpable. The neck was soft and Kernig's sign was absent.

A blood examination showed:—Hæmoglobin—70 per cent. Total W.B.C.—9,012 per c.mm. Differential count: polymorphonuclears—70 per cent, lymphocytes—30 per cent, large mononuclears—0 per cent, eosinophils—0 per cent. Malaria parasite—absent.

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## OBSERVATIONS ON THE MOTTILING OF TEETH IN RATS

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LANTZ and SMITH (1934, 1935) observed that a relatively low intake of fluorine by rats and humans results in no measurable interference with calcium metabolism as determined by balance experiments and yet causes a devastating effect upon the enamel of the teeth when no other symptoms of fluorosis are present. Smith and Lantz (1935) later concluded that fluorine does not exert its characteristic damage to the teeth of rats through its effect upon the enzyme involved in tooth and bone calcification, nor can an increase in plasma phosphatase content be considered a sensitive indication of fluorosis in rats as reported by Phillips (1932) for dairy cows.

Chaneles (1929) reported that the enamel-forming cells are selectively vulnerable to fluoride, being injured by doses for which no other deleterious action has been demonstrated. Histological examinations of the teeth, as carried out by Schour and Smith (1934, 1935), suggest that fluorine exerts a direct local action on the enamel-forming cells, but the recent observations

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The child continued unconscious and developed a slight convulsion at intervals next day. The limbs showed slight rigidity. The general condition was about the same.

On the 13th, there was marked neck rigidity. A lumbar puncture at this time showed purulent fluid under pressure.

The fluid on examination showed a fair number of pus cells and numerous Gram-negative bacilli, which on culture were proved to be *H. influenzae*.

The patient continued in the same condition. The pulse became progressively weak and feeble, and ultimately died on the 16th with signs of peripheral circulatory failure, i.e. five days after admission into the hospital.

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of Irving (1943) do not completely support this view.

A study of the comparative toxicity of the various compounds of fluorine at the same concentration was made by Smith and Levertov (1934). When their effect upon growth, food utilization, etc., in rats was considered, wide differences in the toxicity were noticed among the different compounds of fluorine, such as sodium, potassium, ammonium and calcium fluorides as also sodium, potassium and barium fluosilicates, and the natural cryolite (sodium aluminium fluoride), which might or might not be a reflection of difference in their solubility; but from the standpoint of initial damage to the teeth, all these compounds of fluorine were found to be equally toxic. Recently, Volker *et al.* (1940) explored to some extent the possibility of adsorption of fluorides on the surface of the enamel. To investigate this problem, samples of powdered enamel, dentin, bone and hydroxyapatite were exposed to solutions of sodium fluoride. The amount of fluorine picked up by these calcium phosphates was found to follow the adsorption isotherm, thus demonstrating that fluorine does adsorb on dental tissues. They also conducted a few experiments in which crowns of teeth were dipped for 30 minutes at 40° into solutions of sodium fluoride containing radio-active fluorine. The enamel was partially dissolved off by dipping the tooth into a solution of hydrochloric acid. Small but detectable amounts of fluorine were adsorbed by these intact enamel surfaces; the maximum amount of fluorine adsorbed on a single tooth was of the order of 0.02 mg. These authors conclude that, 'it would be almost meaningless to attempt to differentiate between fluoride adsorption as a physical phenomenon and as a chemical reaction, since there is an excellent chance that fluoride approaching the surface of a hydroxyapatite particle would react to produce fluorapatite (MacIntire and Hammond, 1938; Reynolds *et al.*, 1938; Adler *et al.*, 1938), a mixed apatite, or calcium fluoride (Ercoli, 1939). In fact, the evidence of a surface reaction may have been an artifact contributed by the relatively short exposure of the calcium phosphates to the fluoride solutions (Carnot, 1892, 1893)'.

More recently, Pillai (1942) observed that in the case of rats the external symptoms of mottled enamel disappeared almost completely on changing over to fluoride-free water. In view of this observation of some unique interest and with a view to throwing fresh light on the immediate cause of mottling of teeth in rats and on the course of disappearance and cure of the mottling symptoms, further experiments were carried out, the results of which are briefly described in this paper.

#### *Experimental*

*Effect of elimination of fluoride on the cure of mottled teeth in rats.*—Albino rats (about six

weeks old) were used for the experiments. As far as possible animals of the same litter were used; three from each litter were used for the experiments, while a corresponding number of about the same weight were kept as the control set. In both the sets of the experiments, the animals were placed on a diet including mixed cereals, legume, yeast, casein, minerals and the more important fat soluble vitamins (in the form of shark-liver oil). The only difference between the experimental and the control diets was that, whereas the former was made up with water containing 10 parts per million of sodium fluoride (the animals were also given the same water to drink), the controls were given fluoride-free water. The growth rates of the animals and the conditions of the teeth from time to time were studied.

It was observed that during a period of thirteen weeks there was practically no significant difference between the growth rates of the experimental and control animals. There was, of course, a striking difference in regard to the conditions of the teeth. Two weeks after the treatment the teeth of the experimental animals showed the appearance of pitting and mottling, which gradually developed. As the mottled condition reached an advanced stage by the end of a month, the animals were changed over to fluoride-free water and the consequent changes, more especially on the mottling of their teeth, were carefully observed.

The rate of growth of the experimental animals under the changed conditions as also the difference between the growth rates of the experimental and control rats did not appear to be significant. The condition of the mottled teeth, however, rapidly improved week after week, and about a month after the change over to fluoride-free water, the teeth showed remarkable improvement; and by the end of another month, the external symptoms of mottled enamel disappeared almost completely.

*Influence of diet on the mottling of teeth.*—In order to study the influence of diet (on the basis of Ca-P ratio) on the mottling of teeth in rats, further experiments were carried out providing the animals with liberal supplements of whole milk powder and bone-free fish powder. It was observed that in the case of animals receiving supplements of whole milk powder, the appearance of mottling was delayed and the symptoms did not develop to the same extent as in the other cases.

*Effect of concentration of fluoride on the mottling of teeth.*—As the concentration of sodium fluoride in the water for the experimental animals was increased, the mottling was found to develop more rapidly, and as the concentration of fluoride was decreased, the symptoms correspondingly diminished and slowly disappeared on changing over to fluoride-free water. It would appear that the damage to the incisors of rats, as brought about by the action of fluorine, is repaired at a rapid rate,

so that when the fluoride is stopped the teeth proceed to develop more freely and become normal. The incisors can withstand a higher concentration of fluoride in water.

*Peculiarity of rat incisors.*—The incisors in rats generally grow at a very rapid rate. Thus, when one of the incisors of a four months' old rat was removed, it was replaced to the full size in about six weeks' time. The burrowing or gnawing habit of the animal may have probably a bearing on the fast rate at which the teeth, more especially the lower incisors, develop.

*Experiments with isolated teeth.*—The direct action of fluorine on the teeth has also been studied to some extent by introducing fresh isolated teeth (from rats at different stages of growth) into concentrated solutions of sodium fluoride. Distilled water was used for a similar set of teeth, as a control series. Teeth from young animals were affected rapidly by fluoride, whereas those from older animals being probably more resistant were slowly attacked. The action of fluoride may perhaps be likened to etching observed on glass. Further work is indeed necessary to determine the nature and extent of the direct action of fluorine at various concentrations on the growing teeth in rats.

#### Summary and conclusions

In albino rats, the external symptoms of mottling of teeth as caused by fluoride disappear gradually and almost completely consequent on the change over to fluoride-free water. The remarkably fast rate at which the incisors in rats grow appears to have an important rôle in the mechanism of disappearance of the mottled symptoms.

Concentration of fluoride in water and the diet (presumably rich in available calcium and possibly phosphorus) are two of the important factors that govern the action of fluorine on the teeth in rats.

Experiments with isolated teeth have shown that fluoride exerts a direct action on the teeth. It would appear that the direct action of fluorine is also a factor in the production of mottled enamel.

The authors thank Professor V. Subrahmanyam for his keen interest in the investigation.

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## SEARCH FOR A SPECIFIC CHEMICAL TEST FOR BLOOD STAINS: A COMPARATIVE STUDY OF THE PRELIMINARY CHEMICAL TESTS FOR BLOOD

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No specific chemical test for the detection of blood stains has yet been discovered. A sensitive conclusive chemical test would be of very great value as such a test would not only be a valuable confirmatory test, but would also enable a medico-legal or chemical examiner to examine a larger number of exhibits in a short time. Experiments were, therefore, started in this laboratory for discovering such a specific test, and as a preliminary we thought it best first to study critically the possibilities of the existing more important colour reactions for blood. To find out the limitations of the existing colour tests the work here reported was done to study, (i) the action of substances which simulate the colour of blood, *e.g.* certain fruit and vegetable stains, paints, dyes, iron rust, (ii) the action of substances which are likely to stain seized exhibits (clothes, etc.), *e.g.* saliva, urine, perspiration, seminal fluid, leucorrhoeal discharge, albumin, human milk, cow's milk, soap solution, faeces, colostrum, secretions from throat and nose, pus, and (iii) the action of the commoner acidic and metallic radicles and ions on the more important colour reagents for blood stains. The tests used were the benzidine test, the orthotoluidine test, the leuco-malachite green test, the phenolphthalein test and the guaiacum test for blood. (For the preparation of these reagents and details of the tests see Taylor's *Medical Jurisprudence*, Vol. I, page 463; Sydney Smith's *Forensic Medicine*, page 204. A 5 per cent solution of orthotoluidine in glacial acetic acid and 6 per cent hydrogen peroxide were used for preparing the orthotoluidine reagent. The orthotoluidine test was carried out in exactly the

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same manner as the benzidine test.) The results of these experiments are outlined below :—

(i) The following substances gave strongly positive reactions with benzidine, orthotoluidine, leuco-malachite green and guaiacum, but not with phenolphthalein :—

(1) Potassium dichromate, (2) potassium chromate, (3) potassium ferri-cyanide, (4) potassium permanganate, (5) bromine, (6) calcium hypochlorite, (7) manganese dioxide and (8) potatoes.

(ii) Lead peroxide and iodine gave strong colours with benzidine, orthotoluidine and leuco-malachite green, but not with phenolphthalein and guaiacum.

(iii) Rye and silver nitrate gave positive reactions with benzidine, orthotoluidine and guaiacum, but not with leuco-malachite green and phenolphthalein.

(iv) Formalin and potassium cyanide gave positive reactions with benzidine and orthotoluidine, but not with the remaining reagents. Orthotoluidine gave deeper colours with potassium cyanide than benzidine and was found to be a more sensitive reagent than benzidine for detecting traces of hydrocyanic acid in the atmosphere of a factory, etc.

(v) The following substances gave positive reactions with orthotoluidine, leuco-malachite green and guaiacum, but not with benzidine and phenolphthalein :—

(1) Aluminium chloride, (2) calcium chloride, (3) calcium fluoride, (4) ferrous sulphate, (5) manganese chloride, (6) potassium bromide and (7) potassium iodide.

(vi) Ammonium chloride, banana, iron oxide, lead acetate and potassium iodate gave positive reactions with orthotoluidine and guaiacum, but not with the remaining reagents.

(vii) Bismuth nitrate, calcium carbonate and magnesium oxide gave faint positive reactions with orthotoluidine and leuco-malachite green, but not with the remaining reagents.

(viii) Calcium sulphate, gluten, pleural fluid and potassium bromate gave faint positive reactions with orthotoluidine only.

(ix) Potassium ferrocyanide gave positive reaction with leuco-malachite green and guaiacum, but not with the remaining reagents.

(x) The following substances gave faint positive reactions with leuco-malachite green alone : barium chloride, calomel, phenylhydrazine, potassium chlorate and stannous chloride.

(xi) Apple, betel leaf, black pepper, magnesium chloride, sodium nitrite and zinc chloride gave positive reactions with guaiacum only.

(xii) Chlorine and ammonium or potassium sulphocyanide gave positive reactions with all the five reagents.

(xiii) Besides chlorine and the sulphocyanides, only copper gave strongly positive reactions with phenolphthalein. Copper salts did not give positive results with the benzidine reagent.

(xiv) The following substances gave negative results with all the five reagents :—

Leucorrhœal stains, seminal stains, healthy human faeces (free from blood), animal faeces (free from blood), sweat, nasal discharge (free from blood), sputum (free from blood), urine (free from blood), colostrum (free from blood), human milk, cow's milk, logwood, dyes, orange juice, tomato, guava, sago, soaps, pearl powder, Tokalon poudre, Cusson's talcum powder, Colgate powder, Cuticura, talcum powder, Pond's vanishing cream, Icilma vanishing cream, Tokalon vanishing skin food, methyl red, neutral red, fuchsin, cochineal, oxalic acid, lactic acid, citric acid, gallic acid, tannic acid, pyrogallie acid, sulphanilic acid, phenol, lysol, -naphthol,  $\beta$ -naphthol, aniline,  $\alpha$ -naphthylamine, alum, aluminium phosphate, ammonium sulphide, cobalt sulphate, cobalt nitrate, nickel nitrate, arsenic oxide, antimony sulphide, antimony sulphate, barium sulphide, cadmium sulphate, magnesium carbonate, magnesium sulphate, mercuric chloride, lithium carbonate, lead nitrate, potassium nitrate, potassium hydrogen sulphate, sodium chloride, sodium citrate, sodium acetate, sodium

arsenate, sodium nitrate, sodium phosphate, sodium sulphate, sodium bisulphite, sodium thiosulphate, strontium chloride, zinc sulphate, hydrochloric acid, nitric acid, sulphuric acid, boric acid, ammonia, calcium hydroxide, sodium carbonate, potassium carbonate, sodium hydroxide, potassium hydroxide, coal tar pitch, pure cow ghee, bazaar ghee, mustard oil, coconut oil, red pepper (chillies), prepared pan (betel), coriander, kattha (catechu), turmeric, filter paper, India rubber, rubber solution, starch, sand, gum arabic, gum acacia, gum sandrac, gum tragacanth, resin, clay or earth, sealing wax, this office ink stains, lead pencil marks and copying pencil marks.

**Conclusions.**—It would be obvious from the above that none of the above tests can be regarded as a conclusive test for blood. The great value of these tests, specially of the benzidine test and the phenolphthalein test, lies in the fact that if these tests give negative results, blood is certainly not present, and thus a large number of stained articles may rapidly be examined and those that are negative discarded. Of all the five tests, the phenolphthalein test (for details see *British Medical Journal*, 1926, i, 650) is the most selective, and the benzidine test the most convenient. If a suspected stain gives positive results with both phenolphthalein and benzidine, and if the presence of chlorine and sulphocyanides (which are rarely likely to be present) is excluded, it may be concluded that in all probability the stain is due to blood, for with the phenolphthalein test a strongly positive reaction is seen only with copper salts and blood, and it gives negative results with pus, secretions from throat and nose (unless these contain blood), plant juices, commercial formalin and most of the salts and oxidizing agents which give a positive reaction with benzidine, whilst the benzidine test gives negative results with copper salts. It would, therefore, be worth while to use both these tests as a part of routine procedure for detecting blood stains.

The orthotoluidine test is not so useful as the benzidine test as a sorting test, as many more substances give positive results with this test, but it gives a deeper and more permanent blue colour with blood stains than does benzidine. It is also more sensitive, and in cases of suspected very old blood stains it could be used with advantage in place of benzidine. This test deserves to be better known and should be more widely used as a preliminary test for blood.

The leuco-malachite green test, which Rhodes describes as the most delicate known for blood, was found to be generally not so useful as the benzidine or phenolphthalein test as many more substances (besides blood stains) give a positive reaction with this test than with the latter tests.

The action of these five reagents on very old blood stains was also studied. The orthotoluidine test was found to be the most sensitive test for old blood stains. Orthotoluidine, phenolphthalein, leuco-malachite green and benzidine gave positive reactions with blood stains six years old, but the guaiacum test gave negative results.



## A CASE OF DIAPHRAGMATIC HERNIA WITH MANY COMPLICATIONS

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A BRITISH officer, aged 21, was admitted into hospital with a fracture-dislocation of the 12th thoracic vertebra following a motor accident. He was not unduly shocked, and there was no abdominal rigidity or vomiting at the time. The condition was confirmed radiologically, and he was put in a plaster jacket. There was complete paraplegia corresponding to the 12th dorsal segment, with retention of urine. He was, at first, catheterized, but later a tidal drainage apparatus was set up and his bladder showed progressive increase in tone. His condition remained unchanged until 11 weeks after his accident when one evening he complained of nausea and abdominal pain. His abdomen showed no abnormality, but the chest was not examined. He complained of abdominal pain and vomited all night, and in the morning he appeared distressed and had a bad colour. Temperature 100°F., pulse 130, tongue clean. Examination of the chest showed that the cardiac impulse was in the right nipple line and that there was diminished respiratory excursion of the left chest; percussion gave a tympanitic note, and there was absence of breath sounds in the left chest, no coin sound was detected. The upper abdomen was rigid. His chest had been examined about three weeks before at which time the cardiac impulse was found in the normal place.

It was thought that he had a spontaneous pneumothorax. Radiography showed a left pneumothorax with a fluid level. The mediastinum was displaced to the right, and collapsed lung could be seen in the upper zone.

A pneumothorax refill needle attached to an artificial pneumothorax apparatus was passed through the third left interspace anteriorly. There was a positive pressure of more than 60 cm. of water. The pressure was reduced to normal, but without subjective relief. Accordingly a needle was introduced lower down and 90 c.cm. of odourless turbid fluid withdrawn. He was still distressed, and four hours later 1,090 c.cm. of fluid were taken off with relief. He slept well, and the pulse remained at about 120. The following afternoon the pulse rose suddenly to 160 and was of poor volume. He complained of pain on the left side of the abdomen, and there was marked rigidity and tenderness. He also had frequency of micturition and strangury. It was considered that some abdominal catastrophe

had occurred but surgical interference was deemed inadvisable on account of his bad condition. The pneumothorax apparatus was again connected and the intrathoracic pressure found to be more than 60 cm. of water. Seven hundred c.cm. of air was withdrawn along with 200 c.cm. of fluid, without relief. His condition steadily worsened, and late the same evening 600 c.cm. turbid fluid was taken off. This fluid contained small flakes resembling lymph and was completely odourless. The abdomen remained rigid, and he died three hours later.

### *Post-mortem examination*

*External appearances.*—Body of a young man of average physique. Pale and emaciated.

*Internal appearances.*—Mouth and nasopharynx : nothing abnormal.

Chest : on opening the chest air escaped under pressure from the left side. The left side of the chest was full of straw-coloured turbid fluid with herniated abdominal viscera (stomach, a part of small intestine and omentum and spleen), through an opening in the left dome of the diaphragm. There was no hernial sac. The opening in the left dome of the diaphragm admitted a closed fist. The edges of the opening were smooth. There were no scarring in the diaphragm, no adhesions and no signs of trauma.

Left lung : collapsed except the apical part, which was crepitant and appeared normal.

Right lung : lower part of base congested, otherwise the lung was crepitant throughout and revealed no macroscopic abnormality.

Pericardial sac : no abnormality.

Heart : size normal. Myocardium rather pale and flabby. Right ventricle contained a post-mortem clot. Valves were normal. Coronary orifices patent.

Aorta and large vessels : no atheroma, nothing abnormal of note.

Stomach : there was a perforated gastric ulcer about 1/3rd inch in diameter on the greater curvature about its middle. Mucosa of the stomach congested.

Peritoneum : moderate degree of pelvic peritonitis with straw-coloured effusion.

Appendix was longer than normal but not inflamed.

Bladder : moderate degree of cystitis.

No abnormality in intestines, liver or kidneys.

*Cause of death.*—Diaphragmatic hernia with perforated gastric ulcer in the left side of the chest.

Apart from the paraplegia, this extraordinary case showed the following abnormalities :—

1. Diaphragmatic hernia.
2. Stomach, intestine, omentum, spleen in the left pleural cavity.
3. Perforated gastric ulcer.
4. Hydro-pneumothorax.
5. Pelvic peritonitis.

From the first there were peculiar features :—

1. Failure to restore the mediastinum to its usual place by removal of air and fluid.
  2. The abdominal pain and rigidity.
  3. The turbid appearance of the fluid, different from the usual straw-coloured pleural effusion.
  4. The urinary irritation on the day before death.
  5. The degree of collapse—more than one expects from a simple pneumothorax.
- All these at once raised a doubt whether this was simply a hydro-pneumothorax.



The opening in the diaphragm was thought to be congenital as there was no sign of this patient having an intra-abdominal injury at the time of the accident. Rupture of the diaphragm happens in perforating injuries; in injuries other than perforating wounds where the force is sufficient to cause rupture of the diaphragm one would expect damage to the adjacent viscera with the appropriate physical signs and marked shock. In survival of such cases a certain amount of scarring in the traumatic rent in the diaphragm would be expected. The opening of the diaphragm in this case was quite smooth and without scarring. There were no adhesions and no signs of trauma otherwise in the opening or intra-abdominal viscera. The site of the opening, moreover, is one which is common for congenital defects.

Assuming the defects to be congenital, can the paraplegia have had any effect in precipitating symptoms? It is hard to see how it could have done, as the patient had been completely at rest in bed, and there was no history of any constipation or cough which might have caused a rise in intra-abdominal pressure. Furthermore, he gave no history of indigestion or anything to suggest any abnormality prior to the accident. It is tempting to think that his death was, in fact, attributable to the cord lesion, but very difficult of proof. It is quite possible that disaster would have befallen him in any case.

It is interesting to consider the symptoms in this case in the light of post-mortem findings. The most important lesion, apart from the herniated contents, leading to the fatal issue in this case was the perforated gastric ulcer. It is possible that an ulcer may have existed with insignificant symptoms to which the patient may have attached little importance, but in the absence of any history we also consider it reasonable to presume that the ulcer may have been of acute origin resulting from strangulation of a part of the stomach in the herniated contents, leading to necrosis, ulceration and later perforation. The onset of abdominal pain, nausea and vomiting probably coincided with the perforation.

The air in the pneumothorax was of gastric origin, as also was the fluid, though there was undoubtedly some exudate from the pleura as a result of irritation from the gastric fluid. The presence of abdominal viscera in the thorax explains the failure of the mediastinum to regain a central position, despite the removal of large amounts of fluid and air. The perforation of the gastric ulcer with gravitational peritonitis gave rise to the abdominal rigidity, to the pelvic peritonitis and to the urinary irritation.

This case is related as a pathological curiosity rather than one of practical value. At the same time, it shows the importance of thinking out the genesis of anomalous symptoms in any case—they can never be discounted. It also shows the importance of post-mortem examination in all cases.

## ECHIS CARINATA POISONING

By G. R. PUROHIT, M.B., B.S.

Jodhpur

THERE certainly is a difference between 'snake bite' and 'snake poisoning' or ophitoxæmia, although the term 'bite' is very conveniently allowed to include poisoning as well, whenever it occurs. But, as the name suggests, 'snake bite' should be reserved only for those patients who come with a bite by a snake which is either non-poisonous, or if poisonous has failed either to inject any toxin at all or a sufficient dose of it to cause symptoms of poisoning.

In this part of the country, with its arid sandy soil, the common snakes, or at least the ones for whose bite patients seek treatment, are the vipers, especially the *Echis carinata* or the saw-scaled viper. This is a small reptile known locally as the 'Bandki Pud', measuring usually between one and two feet, but not uncommonly a few inches more than two feet, which during life has a peculiar habit of throwing its body into a double coil and moving sideways, inflating itself and then rubbing one coil against the other producing a hissing sound.

**Symptoms.**—The most important constituent of its venom is that acting on the blood. There is an anti-clotting ferment, a hæmolysin which destroys the red cells, and a hæmorrhagin which is relatively more potent in this than in any other of the Indian snake venoms, and which damages the lining membrane of the blood vessels, therefore frequent and profuse hæmorrhages are distinctive feature of this poisoning.

These hæmorrhages may occur anywhere; thus, there may be bleeding from the gums (which is the earliest and the commonest form I have seen), hæmaturia, melæna, subcutaneous or deep extravasations, etc. I have also come across a patient with a well-marked sub-conjunctival hæmorrhage on one side and another who had blood-stained tears. The other and the less potent component of the venom is the one acting on the nerve cells, especially of the vasomotor centre. It has no direct effect on the central nervous system. Consequently paralyses are conspicuous by their absence.

The local action of the venom is also very severe. As soon as it is injected there is an acute burning pain at the site of the bite, and the part immediately starts swelling; on account of the anti-coagulant nature of the venom, the punctures continue to bleed for a considerable time. The tissues react to it by sloughing, becoming an ideal pabulum for putrefactive germs, and this, I think, accounts for the rise of temperature invariably met with in cases of snake poisoning. Local signs are therefore so unequivocal that their presence or otherwise will give an idea whether venom has been injected or not.

Although conflicting opinions exist with regard to the virulence of echis poison, natives in this

echis-ridden tract consider it to be by far the most poisonous snake, thus conforming to Murray's opinion, 'this little viper is very venomous; although the action of its poison is not quite so quick as that of a cobra, it is equally as potent and numerous deaths annually occur from its bite'.

But much depends upon the dose of the venom injected, whether sub-lethal or supra-lethal, and on the promptness of the treatment received. It is therefore quite possible, as would be evident from the case reports, for a person to be poisoned but to receive a sub-lethal dose of the venom and thus survive without any treatment.

As already stated, the brunt of the blow in echis poisoning is borne by the heart and the blood, and therefore death is usually ushered in by paralysis of the vasomotor centre or by exhaustion from profuse and persistent bleeding, but in this also, I am inclined to think, the place of action depends upon the quantity of venom injected. The larger the dose the more is the likelihood of paralysis of the vasomotor centre ensuing and causing death; and with a smaller dose, the effect is mostly on the blood and the lining membrane of the blood vessels. This latter action of the poison I had frequent occasions to witness.

*Treatment.*—This comes under three heads:—

(a) *Local treatment for the prevention of absorption of the injected venom.*—This is managed by the traditional ligature and incision or excision of the punctures, with rubbing in of potassium permanganate. I doubt very much, however, the efficacy of this procedure especially if, as generally is the case, the patient comes late. Conviction has grown upon me that if a patient seeks treatment after the lapse of about six hours or more, local interference would simply amount to inflicting yet another injury on the one already inflicted by the snake and in fact would prove more detrimental by laying bare tissue devitalized by the action of the venom for germs to grow as also a larger area for free bleeding. Local treatment is thus but a poor consolation. Even if the patient comes with less delay, he has frequently accelerated absorption by running from the place of the accident.

(b) *Specific treatment.*—When the local signs announce the entry of venom, the only treatment is by *intravenous* injection of antivenene (intramuscular injection being just an apology) and 10 c.cm. of the concentrated antivenene should be injected in the first instance, repeated if the symptoms are not controlled. But in echis poisoning antivenene does not seem to have a very marked effect, as in spite of it the action of the toxin on the blood manifests itself.

(c) *Symptomatic treatment.*—As echis toxin has its action on the vasomotor centre, the blood, and the vessel walls, drugs to stimulate the heart, to enhance the clotting and to repair the wall of the blood vessels should be used. Cardiac stimulants and vasoconstrictors to check the

bleeding, such as adrenalin or pituitrin, may be injected, and calcium orally or preferably by injection should be given to hasten clotting and repair of the vessel wall. In theory, such treatments are sound but in actual practice they do not live up to the confidence reposed in them. I have found, however, that in the mofussil where it is not always possible to get proprietary hæmostatic agents, freshly prepared human serum is certainly worth a trial. I have used this in almost all cases with hæmorrhages and with very promising results. Five to seven c.cm. of blood withdrawn from a person's vein and allowed to stand in a test tube for twenty-four hours would yield about 2 to 3 c.cm. of serum. This was injected intramuscularly once or twice a day depending on the severity of the hæmorrhage.

I would now give a few case reports relevant to the points discussed above.

*Case 1.*—A male, aged 20, was admitted into the hospital on 4th June, 1943, about six hours after he was bitten by an echis above the right foot, about 14 miles from here. He ran for about five miles after tying a ligature round the leg. There was a sudden acute burning at the site, and the foot had swollen up. At the end of his five-mile run he started bleeding from the gums. On arrival at the hospital the punctures were freely incised and crystals of potassium permanganate were rubbed in. Intravenous injections of antivenene 10 c.cm., calcium chloride 10 gr., and glucose 20 c.cm. 25 per cent were given and repeated in the evening. By this time he had started bleeding from the nose and the dressing was soaked with blood. Next day all the injections were repeated but the bleeding continued. On the third day the condition was the same and on the fourth day the patient was given an injection of 3 c.cm. serum, the rest of the treatment being omitted. Next day there was no bleeding from the gums and the nose and that from the wound was much less, subsiding completely after two more injections. The wound had sloughed, and the patient had a temperature for about a week. He was discharged cured after a stay of twenty days. In this case even if no incision had been given the patient's life, I do not think, would have been jeopardized. In fact much troublesome hæmorrhage from the wound would have been avoided.

*Case 2.*—A male, aged 45, was bitten by an echis at about 9 p.m. one night and immediately developed pronounced local signs. Next morning at six he attended hospital and was given 10 c.cm. antivenene intravenously, and 30 grains calcium lactate 4-hourly was ordered orally. No local treatment was carried out. Next morning the patient started bleeding from the gums. Antivenene was injected twice daily as also calcium chloride. By the evening, the bleeding from the gums ceased but blood appeared in urine, and there was an extravasation in the tissues of the right thigh. The hæmaturia persisted unabated for a couple of days in spite of injections of calcium chloride, adrenalin and pituitrin. At the end of this period, simply 3 c.cm. serum was injected and the very next day blood in urine was remarkably less; with two more injections the urine cleared. This patient was none the worse for the omission of the local treatment.

*Case 3.*—A male, aged 19, was brought to the hospital early one morning with the history of a snake bite five days back. About six hours after the bite he had started bleeding from the gums and about 14 hours later had hæmaturia and melæna. This continued for three days and then stopped by itself, the patient taking no treatment. The punctures however continued to ooze and the foot and the leg had

(Concluded on next page)

# A PRELIMINARY NOTE ON THE TREATMENT OF 21 CASES OF KALA-AZAR WITH SODIUM ANTIMONY GLUCONATE\*

(WITH SPECIAL REFERENCE TO ITS SUITABILITY FOR MASS ADMINISTRATION ON TEA ESTATES)

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**Introduction.**—The senior writer, Burke (1943), made an appeal for an efficient successor to neostibosan (Bayer), this, preferably, to be a British product. What seems to be an almost perfect answer to that appeal—and indeed a British product—is the preparation stibatin (Glaxo Laboratories), or sodium antimony gluconate (antimony v-hexonate), a crystal-clear sterile solution containing 20 mg. of (penta-valent) antimony per c.cm. which, in collaboration with his assistants, he has recently (August 1943) tested thoroughly in tea estate practice. In such practice it is essential to have an anti-kala-azar drug at hand which is really 'fool proof', e.g. one which is non-toxic, easy and safe to administer (intramuscularly or intravenously), is highly effective as well, and, above all, is

\*This article was accompanied by records of all 21 cases treated, giving details of clinical finding, aldehyde test, differential white cell count, findings of spleen or sternum puncture, details of treatment given, results of treatment and findings on discharge. Space does not permit the publishing of these protocols.—EDITOR, I. M. G.

(Continued from previous page)

swollen up. On admission the patient was absolutely bloodless and prostrate. He could hardly sit up or open his eyes. Temperature 100°F. Pulse 120. Respiration 20. His whole body shook with the impact of the heart against the chest wall. There were blood-stained patches and spots in the skin all over the body. The wound on the toe was covered with a big lump of clot oozing watery serum.

This was in fact a fit case for blood transfusion but as the patient did not agree he was treated with intravenous glucose, massive doses of iron, injections of liver extract and complete rest, and with this he improved. No antivenene was indicated. This patient perhaps received a sub-lethal dose of the venom and therefore could survive without specific treatment. But not all such cases do so well. I have seen two unfortunate victims dying of exhaustion due to profuse bleeding.

On the whole, however, it would appear that one need never lose hope in a case of echis poisoning.

suitable for the mass treatment of a largely devitalized type of tea garden labourer, especially under present war time conditions of great economic stress. It is finally desirable that such a drug be inexpensive. After careful trials and observations, we believe that we have good reason to assert that stibatin is indeed a product possessing the qualities just postulated and, as it is improbable that it has been properly tested to any extent in Assam tea estate practice so far, we are of opinion that the following clinical notes of the first series of 21 cases treated in the Mangaldai district are of sufficient interest, and encouraging enough, to warrant publication.

**Historical.**—The product is not new. It has been used by other workers outside India, but it is, as we have indicated, possibly quite new to Assam. The reports from China and the Sudan, it is stated, have been uniformly good in the past, as well as the original reports—if our memory is correct—from the Calcutta School of Tropical Medicine. Recent work in China gives a favourable impression, but from Calcutta comes an apparently conflicting report by Napier and Sen Gupta (1943) of the School of Tropical Medicine, who in their series of 32 cases of kala-azar treated with diamidino-di-phenoxy-pentane (M&B 800) describe 3 of them (exceptions) which were previously treated with sodium antimony gluconate (not mentioning the maker's name) as follows:—

'In these 3 cases we had previously given a course of injections of sodium antimony gluconate with no effect in case 4, and slight improvement but not cure in the other two.'

We have not placed these cases in the category of "resistant" cases, as the drug used cannot be regarded as possessing anti-kala-azar activity comparable with neostibosan and urea stibamine, and one course of injections cannot be regarded as "ordinarily sufficient" treatment'.

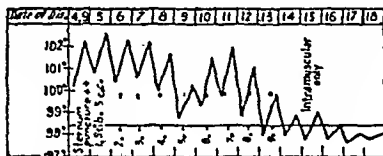
So let it be with stibatin! Whatever deficiencies in therapeutic value it may have had before apart from those reported by Napier and Sen Gupta—of which the present writers are not aware, though they are nevertheless quite willing to be informed of them—the samples placed at our disposal have left no doubt in our minds that a great improvement must have been achieved—if any was necessary—and we are prepared to accord to stibatin a very prominent place in our anti-kala-azar armamentarium whenever mass treatment of tea estate labourers—especially of their children—is required in the future. The present writers are convinced that the Assam species of *Leishmania donovani*, indigenous or imported, is highly and speedily vulnerable to the lethal effects of stibatin. The drug was administered both intramuscularly (an important fact) and intravenously—and by both routes in the same patient in some instances, purely as an experiment—and the results have been exactly the same clinically, irrespective of age, sex, or general physical condition. Cases complicated with malaria, bronchitis, hookworm, etc., were treated symptomatically, and in some



**Blood picture after treatment.**—In all cases except two, there was a marked increase in the hæmoglobin level, at least 15 per cent in 3 cases. A definite leucocytosis was also observed.

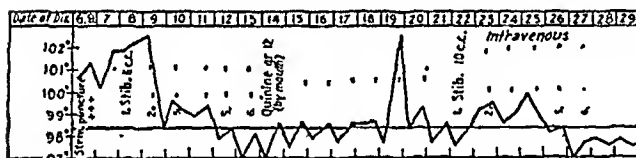
**Weight.**—For various reasons one case was not weighed on discharge, but of the remainder, especially the first 7 of the series, an average of 8 lb. per case was gained on discharge. In 4 cases an average gain of 2 lb. only was recorded.

Fig. 5. Case 5.



Three patients, however, improved with an average gain of 6½ lb. Two hold an individual record of 10 lb. gain each in a month from the commencement of treatment. On the other hand, 3 patients lost an average of 4 lb. each after treatment, although the hæmoglobin percentage was the highest recorded in the series. One lost 1 lb. only but the hæmoglobin increased from 55 to 60 per cent. A discussion on these phenomena would be out of place here.

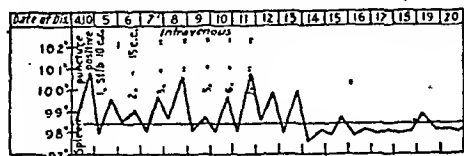
Fig. 6. Case 6.



**Results of treatment.—Fever.**—In most cases the fever dropped to normal after the 4th injection. Cases complicated with malaria, etc., naturally did not follow this course.

Five cases were practically afebrile on admission but had occasional transient rises of temperature (not following any injection of stibatin) which, however, usually soon subsided after a small dose of quinine. Similar observations were recorded by Napier and Sen Gupta in their series treated with M&B 800.

Fig. 7. Case 7.



Two cases only, in our series, were totally afebrile throughout, one of them yielding negative spleen puncture smears, a +++ aldehyde test, but positive sternum puncture smears.

**Spleen and liver.**—In all cases, even with chronically enlarged and hard spleens, remarkably rapid reduction occurred with considerable

softening of the organ. In this respect the results obtained by us with stibatin at least equal those reported by Napier and Sen Gupta in their series treated with M&B 800. The reduction in liver enlargement was equally rapid and gratifying.

Aldehyde tests and spleen puncture smears became negative also, in a very short time. In none of the cases examined after treatment was commenced was a spleen or sternal puncture smear positive after the 14th day. In one case the spleen puncture smear was negative as early as the 10th day. In a few cases the sternum puncture smears were still positive when the spleen puncture smears were negative. No doubt these 'negative' spleen puncture smears may have proved positive if the splenic juice had been cultured.

As regards selection of cases for the series, all were new except 2, one of which had received 10 injections of urea stibamine with no result whatever (and had general anasarca), but when put on to stibatin showed remarkable results, while the other had had 12 injections of urea stibamine also with no result, prior to stibatin treatment. The temperature charts of cases nos. 1 to 7 are of great interest and are very typical of kala-azar, and of the series especially as regards the effects of the injections (see figures 1 to 7).

**Failures.**—In no case was there actual clinical failure in the whole series. With one exception all patients were generally (physically and mentally) much improved, and euphoria was quite definite. This applies also to the 3 patients who lost weight. The single exception is cured of kala-azar clinically, but has a somewhat obstinate anaemia and is still under treatment for this condition (November 1943).

**Findings.**—First of all as regards dosage, as pointed out already, only the first 7 cases of the series were subjected to various experiments in posology, technique, etc., being at headquarters. We therefore did not confine ourselves to the standards laid down by the makers of stibatin. All other cases were, however, treated by one or other of the three standard methods previously described in detail (*vide supra*).

We found that the maximum of 10 c.cm. per individual dose for 6 days recommended by the makers could be safely exceeded in selected cases. It must be remembered that the makers' recommended dosage is an average (or a 'safety') one which must necessarily be laid down, in the public interest, to avoid possible indiscriminate administration by careless practitioners. Having found independently that these limits could be safely exceeded in selected cases, we communicated this, *ad interim*, to the suppliers who replied that the adult dose of 10 c.cm. referred to was not a maximum dose and that larger doses were 'well worth trying'. We did so and, in the first 7 cases, doses of 15 c.cm. were given to patients of 15 years of age, and proportionately large doses to younger



children with perfect confidence. The complete absence of any toxic manifestations, in all cases, has been truly impressive and is a great relief—especially where one is dealing largely with timid, reluctant, and superstitious people who are so difficult, at the best of times, to cajole into submitting to injections of any sort. To conclude our remarks on dosage we must mention that we have found it safe to give, as a single dose, 1 c.cm. per year of age, up to 15 c.cm. (at 15 years), provided that the body-weight at 15 years and over is 100 lb. at least. We believe that 20 c.cm. could be given safely in selected adult cases of higher weight, but we actually consider, at present, that 15 c.cm. is a good maximum average individual dose, having special regard for the general physique of the tea estate labourer patient.

*Discussion.*—These preliminary results have, of course, to stand the test of time, and the cases must be followed up to confirm results of treatment, permanency of cure, etc. At the same time, as far as one's local experience goes, the authors feel that, at any rate, they have in their hands a definitely potent drug of no mean calibre, and of remarkably low toxicity; and, more important still, one that is fairly easily available in India at present. It has certainly saved many children who would certainly otherwise have died for lack of a drug that can be given intramuscularly, as well as intravenously, the former method giving no after-pain whatever. There is no other product available with this qualification at the moment amongst all the anti-kala-azar remedies and, for that reason alone, stibatin must command attention.

Moreover, while, not in the least, attempting to decry the excellent results reported from the use of the non-antimonial, M&B 800, we stress again here, as the senior author, Burke (1943), has already done in these pages, that such products—even in their newest less toxic form—cannot be safely committed to mass administration in ordinary tea estate practice. It may not be out of place either to recall here that an authoritative Editorial in the *Indian*

*Medical Gazette* (April 1942, p. 201) stressed, in its final paragraph, the fact that, after all, it would seem that pentavalent antimony was the best anti-kala-azar weapon at our disposal to-day.

In closing, the writers crave indulgence for any omissions or defects in the notes as presented.

*Summary.*—(1) Sodium antimony gluconate, or stibatin (Glaxo Laboratories), a pentavalent antimony compound, is described and discussed. (2) Treatment of a series of 21 cases of kala-azar is described in detail. (3) It is believed to be as good as any, if not superior to, other antimonial kala-azar remedy the authors have ever tried. (4) Immediate results are remarkably satisfactory, and no great relapse rate is anticipated by the authors. (5) Stibatin is of very low toxicity and can be tolerated in comparatively large doses without ill effects. (6) As far as the usual criteria go, a clinical cure is recorded, at this stage, of 100 per cent of the cases treated in the series reviewed above. (7) It is strongly recommended for mass administration, especially in tea estate practice for reasons given in the text. (8) There is no after-pain with intramuscular use and it is therefore most suitable for children. (9) Stibatin is not at all expensive, compared with most rival antimony products.

*Acknowledgments.*—The senior writer is much indebted to the junior who afforded the greatest assistance in conducting the clinical observations of the first 7 cases of the series, and in compiling and recording all data relative to these, and by preparing the first protocol. Special thanks are due also to the senior writer's other assistants, in various other local hospitals, for their keen collaboration and help with their respective notes, and treatment of their respective 'quota' of cases. They are Drs. M. Chakraborty, P. C. Bhattacharya, B. C. Bose, and R. Aich. Finally, the deepest gratitude is due, and is hereby heartily accorded, to Messrs. H. J. Foster & Co., Ltd., Bombay, agents in India for Glaxo Laboratories Ltd., for their most generous supplies, gratis, of stibatin.

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## A Mirror of Hospital Practice

### ACUTE ANTERIOR POLIOMYELITIS IN ADULTS

By K. N. GOUR, M.D.; M.R.C.P. (Edin.), F.R.F.S.G.,  
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No age can be said to be absolutely immune to acute anterior poliomyelitis but the maximum

number of cases occurs within the first five years of life. Thereafter the incidence gradually diminishes as age advances.

Adult cases are seen in the third and fourth decades of life. They usually occur in epidemics; for example, several cases were met with in the Switzerland epidemic in the years 1923-24 and in 1936. Sporadic cases are very rare. In India, no epidemic of this disease has been reported; the cases are usually sporadic.



The following two cases occurred in adults. They were admitted into the Thomason Hospital, Agra.

*Case 1* (figures 1 and 2, plate XIV).—A Hindu male was admitted on 31st October, 1943, with a history of fever for 10 days, pain in the sacral region and paralysis of both the upper limbs for 5 days. There had been some improvement in the right upper limb but none in the left.

On admission: Temperature 99°F., pulse rate 100; abdomen, cardiovascular and respiratory systems showed no abnormality; cerebellar and cranial nerves normal.

Motor function: There is loss of power in the left upper extremity; wasting of the muscles of the thenar and hypothenar eminences, biceps, deltoid, supra- and infraspinatus, etc. The tone of these muscles is lost and the whole limb is flaccid. In the right upper extremity the tone is a little impaired, and there is slight flaccidity of the limb but there is no wasting.

Reflexes: The superficial and deep reflexes are absent on the left upper extremity; they are present on the right side but sluggish. The organic and sensory reflexes are unimpaired.

#### Laboratory investigations—

1. W.R.—Completely negative.

2. Cerebrospinal fluid:—

Cell count—8 cells per c.mm.

Culture—Gram-positive cocci in pairs and in bunches (probably contamination by staphylococci).

Chemical examination:

Sugar—45 mgm. per cent.

Albumin—fine traces.

Chlorides—800 mgm. per cent.

3. Blood—Total w.b.c.—7,400 per c.mm.

Differential count:—

Polymorphonuclears—70 per cent.

Lymphocytes—30 per cent.

Total r.b.c.—3,850,000 per c.mm.

4. Blood sedimentation rate—60 mm. after 1 hour.  
Blood urea—95.1 mgm. per cent.

5. Electrical reactions:—

On 10th November, 1943—

Faradic response absent in both upper extremities.

Galvanic response absent in both the upper extremities but present in the lower extremities.

On 22nd December, 1943—

Faradic response absent.

Galvanic response present.

6. Skiagram of the spine showed no evidence of cervical rib.

*Progress report.*—He became afebrile on 3rd November. The wasting of the muscles of the left arm became more marked on the 8th, and there was slight oedema on the dorsum of the left hand. The hand was quite cold as compared with the right hand. By the 12th, the right arm was much improved and he could move it freely. Photographs taken on the 15th are reproduced.

*Case 2* (figures 3 and 4, plate XIV).—R. L., 23 years, Hindu male, was admitted on 13th December, 1943, complaining of loss of power in the right arm for two months. He had fever with rigors in September 1943 for about a fortnight. A few days later he began to feel pain in the right arm. The loss of power developed gradually, and now he is unable to move this limb.

On admission: The patient was afebrile. Abdomen, cardiovascular and respiratory systems showed no abnormality. Cerebellar and cranial nerve functions normal.

Motor function: Power is lost in the right arm. There is flaccidity and loss of tone. There is atrophy of the deltoid, supraspinatus, infraspinatus, biceps, etc. There is oedema of the right hand which is cold to the touch. Left arm normal.

Reflexes: Superficial and deep reflexes are lost on the right side.

#### Laboratory investigations—

1. W.R.—Completely negative.

2. Lumbar puncture was done three times but it was always dry.

3. Blood sedimentation rate—6 mm. after 1 hour.

4. Blood calcium—8.8 mgm. per cent.

5. Uric acid in blood—3.3 mgm. per cent.

6. Electrical reactions:—

Faradic response present in the right upper extremity, comparatively weaker.

7. Blood—Total r.b.c.—4.2 million per c.mm.

Total w.b.c.—8,000 per c.mm.

Differential count:—

Polymorphonuclears—81 per cent.

Lymphocytes—18 per cent.

Large mononuclears—1 per cent.

The symptoms and signs in both the cases suggest the probable cause to be that of acute anterior poliomyelitis. Though acute spinal atrophic paralysis may occur in other infectious diseases. *e.g.* influenza, typhoid fever, etc., the history and clinical examination in both the cases were against them.

#### Comment

1. Two cases of acute anterior poliomyelitis in adults have been reported.

2. Case 1 shows that both the upper limbs had been involved but the right upper limb gradually improved in motor power and within about three weeks' time it was quite normal.

Case 2 showed involvement of the right arm only.

3. Both the patients developed oedema of the hands of the paralysed side showing trophic changes.

4. In both the cases the upper limbs only were affected.

5. No contracture was seen in either of the cases.

6. In case 1 electrical massage improved the nutrition of the paralysed muscles but not in the other.

I wish to thank Major-General H. C. Buckley, M.D., F.R.C.S., C.S.I., I.M.S., Superintendent of the Thomason Hospital, for allowing me to publish the above two case reports.

#### CORRIGENDUM

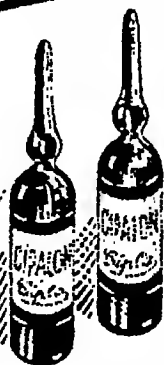
In the article entitled 'Some Common Misconceptions of Malaria' by John Lowe, published in the May number of the *Gazette*, p. 207, the first three lines of the second paragraph were inserted at the bottom of the left hand column at the end of the previous article, instead of at the top of the right hand column, as passed in the final proof.—Editor, I. M. G.

# HIGHLY POTENT WHOLE LIVER EXTRACT

HG %	RBC count
100	5
90	4.5
80	4
70	3.5
60	
50	
40	
30	



2cc. 2cc. 2cc. 2cc. 2cc.



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PRIMARY  
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## Indian Medical Gazette

JUNE

### FLUORINE AND FLUOROSIS

FLUORINE is one of the trace elements that are normally present in our body, and in small quantities it is believed to exert a beneficial influence. It is so widely distributed in nature that a small intake of the element is unavoidable. It is present in drinking water and many of our foodstuffs, and was at one time frequently used as a preservative, although its use as such is now prohibited in most countries. Certain insecticides and fumigants contain fluorine, and industries, such as mining and the conversion of phosphate rock into superphosphate, a common fertilizer, and the manufacture of glass, enamel and aluminium, expose workers to appreciable dangers of excessive fluorine intake. Prolonged ingestion of abnormal quantities produces a chronic toxic state, the earliest visible sign of which is hypoplasia of the teeth often described as 'mottled enamel', 'chronic dental fluorosis', etc. Its commonest source is drinking water, and the level above which effects are produced is about one part per million, equivalent to 1/120 grain of fluorine to a pint of water. It was first noticed in cattle grazing near a superphosphate factory in Italy, and it has since been recognized in farm animals in many places. The affected animals show lameness, thickening of bones and cachexia, and analysis of their urine and bones shows an increased amount of fluorine. The bone marrow is considerably reduced.

The first account of mottled enamel in human beings was given in 1902 by Eager of the United States Public Health Service who noticed its frequency among Italian emigrants from Naples. Black and McKay (1916) found it occurring in various parts of the U.S.A. and described it more fully in 1916. Since then, cases have been reported from every continent, but although popular belief associated the condition with drinking water, it was not till 1932 that fluorine contained in it was established experimentally by Smith and her associates, as the aetiological factor. Its recognition in India is more recent. In 1936 the health authorities noted a peculiar disease in the Nellore district in Madras Presidency, which was characterized by stiffness and pain in the spinal region and in various joints. A preliminary survey revealed the presence of fluorine in the drinking water of the district and a heavy incidence of mottled enamel in the teeth of school children, and subsequent investigation showed that both these conditions were present in several other districts as well.

The average fluorine content of water in the endemic areas is well over the threshold level,

it being derived from the fluoride-containing strata of earth. The depth of the wells does not appear to have any connection with fluorine concentration, but sometimes it has happened that the substitution of deep well water for that of shallow wells for sanitary reasons led to the occurrence of mottled teeth. It may be stopped by changing to a water supply containing fluorine less than one part per million. Even before the discovery of the causative agent it was not uncommon for people to abandon otherwise satisfactory water supplies, feeling that the water was responsible for the defective enamel formation. In Madras, sometimes whole villages moved from one site to another in search of better water.

Fluorine is a normal constituent of our teeth and bones, and in chronic poisoning these structures suffer most. Mottled enamel is one of the first signs and is seen in people who, during the period of calcification of the enamel, have resided in an area with high a fluorine content in the drinking water. The process is naturally slow in appearing and in progressing. The outer surface of the front teeth is usually most affected, showing opaque paper-white patches or horizontal bands of varying widths. Sometimes the whole surface loses its normal glossy translucency and assumes a dull chalky white appearance. Later, the whiteness is replaced by brown or yellow, occasionally black, markings. As the condition progresses, pits appear. Histologically there appears to be a lack of cementing substance between the enamel rods. The discoloration is described as due to deposit of a pigment in the interstices between the rods. The teeth are of normal shape. The severity of the lesions increases with the concentration of fluorine in the water and the length of time of its ingestion. Normally there is no effect on general health, and in very mild cases there may be nothing more than some white spots. The mottled teeth contain more fluorine than carious teeth, and American work has suggested that they are less prone to caries, and work in England seems to bear this out. This has led to the suggestion that non-toxic amounts of sodium fluoride may be added to drinking water for the prevention of dental decay.

Endemic dental fluorosis occurs in many parts of the world, but cases with skeletal changes seem to be comparatively rare. They were first observed by Flemming Moller and Gudjonsson (1932) in cryolite workers near Copenhagen, who had been exposed to fluorine for long periods. Cryolite, a double fluoride of sodium and aluminium, containing as much as 54 per cent of fluorine, is used in the manufacture of aluminium. Besides showing some anaemia and dyspeptic symptoms, many of these workers had restricted mobility of the spine, and in severe cases almost complete rigidity. Radiography showed a progressive sclerosis of the bones, especially of the vertebrae, pelvis and ribs, with calcification of the costal cartilages. In

typical radiograms the osseous pattern is completely effaced, the bones appear marble-white and structureless and their contours are irregular. The attachments of muscles become thickened and ossified, and there is considerable ligamentous ossification, especially about the intervertebral and costo-vertebral articulations. In a study of some advanced cases in Madras, Shortt and his colleagues (1937) found similar changes in the bones, the clinical picture resembling spondylosis deformans, but the articular cartilages were not affected. They also observed that the bone changes appear in adults usually preceded by symptoms, such as general tingling sensation in the limbs and body, followed by pain and stiffness, especially in the lumbar spine. The stiffness increases until the entire spine behaves like a continuous column of bone. The ribs become fixed and the breathing entirely abdominal. The final stages of the condition are generally evident in people past forty; there is definite cachexia with complete rigidity of the spine and joints, the patient becomes bedridden, and dies of some intercurrent disease. Such severe cases are restricted to villages with a high fluorine content in water (about 6 parts per million). Similar lesions have also been reported from South Africa.

It is not known whether the bones begin to be affected at the same time as the teeth. Kemp, Murray and Wilson (1942) made a preliminary enquiry in some English villages to find out whether the fluorine in the drinking waters, while sufficient to produce dental fluorosis, caused any skeletal changes during the growing period which might lead to incapacity in later life as seen in other countries. They found early signs of spondylosis deformans in some children and young adults, but the correlation was by no means definite. The authors believe that fluorine may favour the development of such defects, but probably there are other factors as well, such as defective nutrition. This is borne out by the work of Pandit and his colleagues (1940) who found that the incidence and severity of the disease had a definite relation to the economic and nutritional status of communities, and that the two important factors concerned in the production of severe chronic fluorine intoxication were the high fluorine content of water supplies and deficiency of vitamin C in the diet. A diet rich in calcium, phosphorus and vitamin D has been reported to have a beneficial influence on the condition. There is no doubt that economic conditions are the factor responsible for the rarity of advanced bone changes in countries such as the U.S.A. and England.

Elsewhere in this issue we publish two articles in which Pillai, Rajagopalan and De record the remarkable protection afforded by whole milk powder (klim) against fluorine poisoning in experimental rats. They also found that a supplement of bone powder in their diets gave considerable relief to the symptoms of intoxication such as stiffness of limbs, difficulty in free

movement, etc. These results, they think, may be due to their calcium and phosphorus contents. A reduction of the concentration of fluorine with improvement of the diets gradually produced a beneficial effect on the mottling of the teeth as well. Fluorosis can be such a crippling disease that it is worth testing these observations in human beings.

R. N. C.

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## Special Article

### SOME TROPICAL MEDICAL PROBLEMS IN SURGICAL CASES\*

By G. F. TAYLOR  
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In the surgery of tropical medicine, two stages are passed through. The recently arrived surgeon in India tends to operate without consideration of such diseases as amoebiasis which mimic surgical conditions of European practice; also he tends to overlook the effects of a hot climate. After initial mistakes, there is a tendency to diagnose tropical diseases when they are not present, and therefore to hesitate to operate on such surgical condition as acute appendicitis. The co-operation of physicians and surgeons is needed in all hospitals, not only for acute cases. A regular round by a physician of the surgical wards is a good routine in the tropics.

Unfortunately, there is not, as far as I know, a recent good book on the surgery of tropical diseases.

*Climatic effects.*—The effects of heat need equal emphasis both in the surgical and medical wards. Hyperpyrexia, dehydration, hæmo-concentration and circulatory failure are frequent

\* Being a paper read at the Surgical Convention in Calcutta on 6th September, 1943.

causes of trouble. The effects of heat have been well described in the Medical Directorate of India's bulletin no. 15 of April 1943, which all medical officers, surgeons and physicians should read. Briefly, there are two kinds of heat effects: (a) heat exhaustion due to water, and/or salt deficiency, (b) heat stroke, or overheating due to stopping of sweating, associated with such conditions as infections, surgical operations and so on.

In medical wards, dehydration and salt depletion have been very common, often due to patients not being given frequent and abundant fluids by the mouth. Shortage of nurses is partly responsible, but medical officers have not stressed the importance of very frequent fluids.

In medical wards a bottle of water or a canvas 'chagul' by each bed containing fluid with  $\frac{1}{2}$  ounce of salt to the gallon, with a rubber tube to act as a 'straw', has been found useful and should be a routine for all seriously ill patients who can drink.

After operations, we want to know in all cases that enough water and salt has been given. The best guide to this is the quantity of urine passed and its salt content. An easy method of measuring the daily urine is to mark a rum bottle to a level of 4 pints, which is about the half-way mark, and for each specimen of urine to be poured into the bottle. At the morning round, the surgeon can see for himself if the quantity of urine passed is adequate or not. He can also have the urine tested for salt content, by the simple method given in bulletin no. 15. If the patient is badly collapsed, treatment should be controlled by—

- (a) the general condition of patient,
- (b) the blood pressure taken half-hourly,
- (c) the urinary output and salt content measured 4-hourly.

The aim should be to attain an output of  $\frac{1}{2}$  pint 4-hourly and a salt content of 5 to 10 grammes per litre. Some surgeons in the tropics give a routine intravenous saline in all cases after operation, to which quinine can be added, if need be. Hyperpyrexia is a common occurrence after operation. If there is any doubt of malaria, quinine must be given at once. Then the essential treatment is to cool the patient by evaporation of water from his skin, by fanning the body. The temperature should be taken every 10 minutes until it is down to 102°F.

Lumbar puncture, to reduce the C.S.F. pressure to normal, is of use. The cold room helps in treatment as well as in prophylaxis of hyperpyrexia.

Again, emphasis is needed by us all that the quantity of urine passed and its salt content should be checked in all seriously ill cases, whether surgical or medical, particularly in cases with vomiting or diarrhoea.

Obviously drugs of the atropine group which inhibit sweating should be avoided. When patients are unconscious during and after operations, care should be taken not to prevent their

normal heat loss by over-covering with bed clothes and by the use of rubber sheets.

The increased liability of the skin to become septic in hot weather, particularly towards the end of it, is realized after experiencing one or two hot weathers in India, especially in the hot humid Bengal climate. A visit to the skin wards will convince the septic of the greater frequency of boils, carbuncles and of the septic condition with or without prickly heat. Fungus infections are much more frequent and have led to very unpleasant extensive infections under plasters. In my experience there is an increased European death rate at the end of the hot weather. There is no name for the cause for this and there is nothing we can measure, except possibly a lowering of the blood pressure. The blood pressure in Indians is, as you know, lower than in Europeans—and in Europeans in India; the blood pressure is commonly 5 to 10 mm. below the European level, and the weight is an average of 10 lb. or so below English standards. In the past, we have said the patient has been fagged out by too many hot weathers. The regular taking of leave after 2 or 3 years has helped to prevent it developing. It is a pity there is no 'fag index' we doctors could measure, to know when the danger point is reached.

I have questioned whether the hot humid climate of Bengal is the right place for neuro-surgical and facio-maxillary work. Also, if the war goes on for several more hot weathers, would not better surgical results be obtained by sending as many surgical cases as can travel to the cooler climate of a hill station for operation and convalescence? In the past, operations have been avoided during the hot weather and cases sent, if not to England, anyhow to a hill station.

Urinary disease in hot climates is considered later.

The treatment for shock has been worked out in temperate climates. All wound casualties after a few hours in a hot climate are very dehydrated and need urgent treatment for the dehydration complicating the shock; this has not been sufficiently emphasized.

*Malnutrition.*—How far malnutrition interests and concerns the surgeon you may be able to say. There is no exact definition of malnutrition. In British troops there is the loss of weight which is usual in most Europeans in India. There have been many cases of vitamin B<sub>2</sub> complex deficiencies with glossitis caused by the lack of absorption due to diarrhoea, dysentery, and early and developed sprue.

In Indian troops the malnutrition has been a more serious problem. Many have not been able to stand up to the strain of severe malaria and, in many cases, of hookworm infection. In July patients began to be admitted into hospital complaining of anorexia and flatulence, soreness of the tongue and mental apathy. They have a red superficial glossitis, develop severe anaemia and diarrhoea with great loss of weight.



Examination of the blood shows a low plasma protein, the albumin being much lower than the globulin. The condition appears to be a pre-pellagra condition. Some troops in the area on full duty have minor degrees of this condition, such as a sore tongue. Scurvy and other deficiency diseases have been uncommon. These deficiencies of the B complex, of protein; and of vitamin C are connected with wound healing, wound and skin sepsis, and the union of fractures. According to Whipple, chloroform anaesthesia is more dangerous in cases of hypoproteinaemia.

There is a further point regarding the so-called 'Naga' sores. Last year, they were very much more common than this year. Last year, the rations for British as well as Indian troops in forward Assam areas, during the monsoon, were deficient in fresh supplies for longer periods, and sores were alarmingly common.

The addition to the diet of protein, fresh fruits and vitamins in surgical cases, and the elimination of such debilitating diseases as malaria, anaemia, round- and hookworm, and chronic amoebiasis is part of the essential treatment of all surgical as well as medical cases. We have been taught that, as far as is possible, symptoms should be traced to one source. In tropical medicine this is often impossible.

*Malaria.*—The extent of malarial infection is under-estimated by the figures of hospital admission, because many cases are never admitted into hospital, and receive 'blanket' or other treatment in their lines.

It is unnecessary to describe the ordinary attacks, but a word is needed on suppressive treatment and the so-called latent malaria. Troops in highly malarious forward areas in jungle warfare cannot use nets, and are now on suppressive mepacrine. As the name implies, this suppresses but cannot knock out the infection, which, because of the conditions under which troops operate, is present in practically 100 per cent of the men. When the suppressive mepacrine is stopped, clinical malaria develops in practically all the men, within a few weeks (usually two), as the parasite can develop in large enough numbers to produce the clinical attack, unless a course of so-called blanket treatment is given. This is designed to knock out the infection, which unfortunately it often fails to do. When men taking suppressive mepacrine are wounded, they have often stopped taking their mepacrine. They then rapidly develop malarial fever to complicate their surgical condition. The rule which all of us must follow is to make sure that all hospital admissions, surgical and medical, continue with suppressive mepacrine until they are evacuated out of the malarious areas, when they should receive a course of blanket treatment.

Many men, in addition to those on suppressive treatment, are carriers of malarial parasites. For example, in a group of men from an expedition recently, over 75 per cent were found to harbour parasites, with no clinical fever. Any

shock, infection or wound may bring out this latent infection and produce an attack of fever. You are all familiar with attacks of malaria following operations. Many surgeons working in highly malarious areas make it a practice to give quinine as a routine just before and after operations.

Although malaria commonly causes a sharp attack, it may produce almost any type of fever, and must be borne in mind in all cases of fever of uncertain origin.

It may, and commonly does, complicate any medical or surgical condition. The underlying cause of an accident producing a fractured base or a subdural haematoma may have been an early cerebral malaria, which needs more urgent treatment than the fracture or the haemorrhage. The problem arises in such cases as to which symptoms are malarial, but if there is any doubt of malaria being present, quinine must be given, if need be, by intravenous injections. Of course there is the danger of attributing too much to malaria and missing acute appendicitis or a subdural haematoma which needs urgent operation.

Malaria, especially M.T. malaria, can produce symptoms in any part.

It can mimic acute abdominal conditions in producing fever, vomiting, localized abdominal pain and tenderness, with sometimes localized rigidity which can be distinguished from a surgical condition by the clean tongue, the usual slighter rigidity; and the absence of a raised white cell count. It can lead to internal haemorrhages, as well as to dysentery, while a slightly enlarged tender liver is commonly seen in the malarial attack. In England we have been taught that normally the liver is not palpable in health. In British troops in India, in the experience of many, the liver is commonly found to be enlarged without obvious disease, and in Indian patients it is almost the rule to be able to palpate the liver in normal health. This is probably due to previous malaria or intestinal infections or occasionally infective hepatitis.

Rupture of the enlarged malarial spleen has been recorded commonly after blows and accidents, but it can and has occurred recently in this Army during an attack of fever without any external violence.

In transfusion, the donor may develop malaria as the result of giving his blood and the recipient may be infected by the donor's blood. A recent *Medical Annual* records a case of quartan malaria transmitted by transfusion 17 years after the donor had been exposed to malarial infection. Hence in Eastern India, both donor and recipient need treatment for malaria as a routine, as it is impossible to be certain the donor is free from infection.

Recently, Major Davies has brought to the notice of the transfusion authorities that an appreciable number of donors, it is either 3 per cent or 5 per cent, are found to have positive

Wassermann, but they receive neither a report of this, nor investigation, nor treatment.

The question has been raised whether the livers of men on suppressive mepacrine are damaged, so that anaesthesia is made less safe than usual. As far as I have seen, there is little evidence to support this damaged liver idea, but the effect of suppressive mepacrine on liver function needs more detailed investigation by a biochemist.

Anæmia associated with malaria, hookworm and malnutrition is almost universal in Indian troops in forward areas, and needs investigation in each case to decide on the right treatment.

In medical wards, the blood transfusion of severe Indian anæmias has given rise to a high rate of reactions (one officer reported 80 per cent reaction rate), with more than a dozen deaths in Eastern Army immediately following, and presumably caused by, the transfusion. The transfusion units are investigating the matter. There is some evidence that the cause is faulty cleaning of apparatus in damp humid climates, leading to the growth of moulds. Both surgeons and physicians need an early solution to this problem so that transfusion may be given with confidence.

*Amœbiasis.*—It is impossible to be certain of the incidence, but in Eastern India it is very high and will be worse in the future as troops move eastwards where the carrier rate is one of the highest in the world. Recently, in Calcutta, a group of B.O.R.s doing ordinary duty were examined. Over 25 per cent were carriers of cysts, and just under 10 per cent were carriers of vegetative amœbæ.

From the surgical aspect, it must be remembered that chronic amœbiasis causes fibrosis and thickening around ulcers, commonly in the sigmoid and cæcum, localized polypoid formations of the mucous membranes, localized peritonitis, and perforation of ulcers, and that the appendix is involved in 41 per cent of post-mortem examination (Clark); also when the liver is involved in amœbic hepatitis, that abscesses may be multiple, and that infection may spread through the diaphragm, causing immobility of the diaphragm and effusion in the pleura.

There is no time to go into details of chronic intestinal amœbiasis, but everyone will, I think, agree that amœbiasis needs excluding in most common intestinal surgical conditions, before operation is decided on. This is done by a careful history, examination of the stools and a sigmoidoscopy in which material is taken from any visible ulcers and examined for amœbæ. The examination for amœbæ may have to be repeated several times.

The observation of Colonel James, that the commonest site for a single amœbic ulcer in chronic amœbiasis is  $5\frac{1}{2}$  inches from the anus, interests me because among physicians there is a debate whether the proctoscope can replace the sigmoidoscope.

The common conditions when amœbiasis must be considered are thickened and often tender lumps in the cæcum and sigmoid, mistaken for carcinoma or tuberculosis, in acute and chronic appendicitis, in stricture of the large intestine and rectum. Piles often complicate chronic amœbiasis. There have been many examples in this Army of all these conditions, where the underlying amœbiasis has been missed in diagnosis. Hæmorrhage from the intestinal tract may be from an amœbic ulcer, and localized peritonitis from a small perforation. It is agreed that amœbic cases of this type if operated on in the acute stage all do badly. The amœbic appendix, if removed because of a mistaken diagnosis of an acute septic appendicitis, leads to a fæcal fistula, and the stitches round a perforation cut out. Both have a high mortality rate. Surgeons with experience of these conditions, I think, agree that a course of emetine is essential before operation, and that if the plum-coloured cæcum characteristic of amœbiasis is found on operation, the abdomen should be closed without further interference, and emetine begun.

On the other hand, ordinary surgical conditions needing immediate operation such as acute septic appendicitis occur in cases of chronic amœbiasis. The decision to operate must be made after a full consideration of the history and clinical findings, including a sigmoidoscopy and examination of the material from ulcers. You will be discussing these conditions in detail at this conference and possibly will be able to lay down more definite indications for operation and the treatment of the accompanying shock and sepsis, by plasma transfusion and possibly the sulphur drugs.

Amœbic hepatitis and abscess is a concern of both surgeons and physicians. The diagnosis can be easily missed and mistaken for carcinoma of the stomach, diseases of the gall-bladder and kidney, sub-phrenic abscess, liver disease such as hydatid, infective hepatitis, gumma and cancer. Above the diaphragm, pleural effusion and empyema are a common cause of trouble. The shoulder pain has been mistaken for rheumatism. One of the common mistakes in Indian civilian practice is to diagnose and treat the enlarging tender liver of congestive heart failure as amœbiasis, with emetine, with disastrous results to the heart muscle. I have seen several mistakes in cases of pleural effusion, pushing the liver downwards and rotating it forwards. Tapping the effusion allowed the liver to return to its normal position. The slightly enlarged liver so commonly seen in both British and Indians, especially if it is further enlarged by alcohol, has often had unnecessary emetine treatment. There is no golden rule to guide us. Amœbic abscesses may produce no fever, and no raised white cell count, and 50 per cent have no amœbæ or cysts in the stools. X-ray photography is obviously of great help, but again mistakes are common. The inner 'leaf' of the diaphragm is slightly raised above the curve of

the dome in 20 per cent of normal people, and is a common source of error.

The question of aspiration and operation always arises. It can, I think, be taken as decided that, wherever possible, emetine should be given a trial for at least 4 days before aspiration, as it is astonishing how often emetine will clear up enormously enlarged and tender livers. It has been shown in tuberculosis that a common cause of pleural effusion after the production of an artificial pneumothorax was the small disc of skin, punched out by the A.P. needle, and pushed into the pleura. One of the common causes of secondary septic infection of amœbic abscesses is the small disc of skin, or the needle infected by skin, pushed into the sterile abscess. The skin after careful preparation must be nicked with a sharp knife, through which the needle is inserted.

If the condition does not improve after aspiration, remember that multiple liver abscesses are common and may need a second or several aspirations. The pus from a liver abscess, normally sterile, should be cultured for secondary infecting organisms. If they are found present, a course of sulphathiazole should be tried with emetine. Open drainage may then be necessary. In the past, the secondarily infected abscess often came to open drainage, with a high mortality, but sulphathiazole or newer drugs may improve the outlook. Open drainage of an amœbic abscess is as unjustified as open drainage of an abscess from a tubercular spine.

*Other abdominal conditions.*—Tuberculosis of the abdomen, often with no obvious chest infection, is commoner in some Indian races than in Europeans. In the Punjab, it is taught that the commonest cause for abdominal pain, after intestinal colic, is abdominal tuberculosis, particularly in young adults. Cases of glands round the cæcum and cæcal tuberculosis going on to incomplete obstruction are much common than in English wards. The cause of this is unknown and is being investigated in Lahore.

Hookworm in Indians is present in over 50 per cent of admissions into most hospitals of this Army. It causes not only anæmia, but worms in the duodenum may cause symptoms resembling a duodenal ulcer, which are cleared up by a hookworm treatment.

Colonel Crookshank has pointed out that santonin is another drug which can cure some cases of intestinal obstruction. Round worm infection in South Indians is very common, and cases have occurred recently in the Army in which a mass of round worms have been removed post mortem from cases operated on for obstruction.

Infective hepatitis has given rise to difficulty in the first few days, with its vomiting and liver pain and tenderness, before the jaundice has appeared. The general aches and pains of dengue have in one case led to the abdomen being unnecessarily opened. Perforations in typhoid need no emphasis, except that their mortality is

always very high, as in the perforation of bacillary dysentery, when the gangrenous state of the gut may be mortal.

Appendicitis is less common in Indians than in Europeans, but it is not anything like as uncommon as Manson-Bahr's statement of seeing two cases in Indians in 30 years, leads us to suppose. He was practising in England! It is thought to be less common in Indians in villages than in towns, but I know of no figures to prove this.

*Sulphonamide in surgery.*—This conference would do well if it lays down principles for the use of sulphonamide. The following seem important:—

(1) A bacteriological examination to find the causal organism. Recently, in the notes of a surgical case, a few tablets of proseptasine were given for a septic sinus, from which staphylococci were discharging.

(2) An initial large dose of the selected sulphonamides to produce the optimum action.

(3) A smaller maintenance dose repeated 4-hourly.

(4) The period in which the drug is used should usually be 5 to 7 days (except in the cases of sulphaguanidine, when longer periods are recommended for chronic bacillary dysentery) as organisms acquire a tolerance to sulphonamide.

(5) A second course can be given after 5 to 7 days' rest.

(6) A leucocyte count is needed 3 days after beginning of a course and before repeating a second course, to make an early diagnosis of a possible agranulocytosis.

(7) The skin needs watching for skin rashes.

(8) The main serious complications of sulphonamides are due to their deposit in concentrated urine in the tubules of the kidney, leading to hæmaturia and anuria. These usually can be prevented by ensuring that the patients pass 4 pints of urine in 24 hours. This is vitally important in hot climates. The best way of doing this is to measure the urine output by collecting it in a rum jar, marked to a level of 4 pints, and seen each day at the M.O.'s round, when it is emptied. An intake chart is valueless. Any sign of hæmaturia and anuria means that the drug should be stopped. The earliest signs of trouble are a diminishing quantity of urine and the presence of red blood cells in urine. The earliest complaint is often pain in the loin or supra-pubic region, which may be the first sign of danger.

(9) Alkalis have been said to prevent urinary complications. For sulphapyridine, alkalis are useless as there is no increase in solubility until a pH of over 9 is reached, which is not obtainable in urine. Sulphanilamide has not been reported as causing obstruction. Sulphadiazine and sulphathiazole are only slightly soluble in urine with a pH below 7. There is a tenfold increase in solubility between a pH of 6.7 and 7.5, so that alkali should be used with these

drugs. 10 to 20 grammes of bicarbonate are needed to keep the urine pH above 7.0. Alkalis may be of use in preventing vomiting.

•(10) When anuria has developed, this conference may be able to decide when is the best time to operate after intravenous sodium sulphate and other treatments have been given, and what best should be done. For renal lavage in obstruction cases, a strong solution of bicarbonate should be used.

(11) Other complications such as vomiting, hæmolytic anæmia and jaundice have not the importance of the urinary complications.

(12) Sulphonamides are comparatively useless when pus has loculated in serous cavities or in bones. Their use may mask the need for operation. Recently, a case of brain abscess which had been treated came to post-mortem examination. The symptoms had diminished under the sulphonamides, and the brain abscess was not diagnosed. I understand the aural surgeon is finding the same difficulty in deciding when to operate on mastoids.

Four years ago when sulphapyridine first came in, I treated 17 consecutive cases of pneumococcal empyema with M&B 693 and aspiration, endeavouring to avoid open drainage. It was found, if the pus was merely turbid, that cases would clear up without open drainage. When the thick pus had formed, aspiration and repeated courses of M&B 693 for periods up to 3 months did not clear them up, and an open operation had to be done.

(13) Sensitivity of the skin to sulphathiazole needs consideration.

#### *Other tropical medical conditions of importance to surgeons*

*Enlarged glands.*—Acutely enlarged and tender glands occur not only in plague but in typhus of the OXK type. A recent series of cases in Assam had masses of enlarged glands all over the body. Filaria is common in Eastern India and an eosinophil count and search for filaria in the blood taken at night should be done in all cases of enlarged glands, of hydrocele, varicocele and lymphangitis. Tuberculous glands are possibly more common in Indians than in British.

*Kidney conditions.*—Renal colic due to crystals deposited in the concentrated urine resulting from sweating and a small fluid intake is very common. You have a special series of papers on this subject. It is often very difficult to decide whether or not a small stone has formed, but I think the surgeon is often too ready to pass catheters up the ureter of such cases. The prevention of renal colic and renal stones needs emphasis.

*Bone and joint conditions.*—Dysenteric arthritis due to bacillary infections is fairly common. It needs M&B 693 treatment in addition to the usual treatment for the acute arthritis. Typhoid spine and typhoid periostitis have occurred in

several cases. The spread of fungus infection and sepsis under plasters in the hot weather has already been mentioned.

*Skin conditions.*—Cellulitis of the feet may often begin from an epidermophytosis between the toes. Oriental sore is uncommon in Eastern India. Kala-azar extends to about as far as Lucknow. Further west, kala-azar is almost unknown in India except in cases imported from Eastern India, while oriental sores are excessively common in the Punjab and further west. The reason for this is, that the two diseases are transmitted by different varieties of sand-fly, in moist areas, kala-azar by *Phlebotomus argentipes*, and in dry areas oriental sore by *Phlebotomus papatasi* and *Phlebotomus sergenti*. For some years in Lahore oriental sores had been treated by the intradermal injection of atabrin and mepacrine. Three c.cm. of a solution of one tablet dissolved in 5 c.cm. of sterile water are injected intradermally in three sites round and into the sore. Two or three of these injections repeated at weekly intervals clear up nearly all oriental sores. There is a description of this method in a recent *Indian Medical Gazette*. Scores of patients have been treated with this method in Lahore with better results than with berberine or any other treatment.

*Nervous conditions.*—Leprosy is very common in Eastern India. It is often forgotten, as Dr. Lowe has pointed out, as the commonest cause in Indians for foot drop, wasting of the hand muscles and facial paralysis. In a recent case which had been diagnosed as infantile paralysis, Dr. Lowe was able to find an enlarged external popliteal nerve. Infective neuritis has occurred too, causing foot drop with some sensory loss and has been confused with polio. In 1942 there were several scores of cases of diphtheritic paralysis following secondary infection of 'Naga' sore with diphtheria, but so far these cases have been rare this year. Cysticercosis occurs commonly here in Bengal, but so far I have not seen a case in the Eastern Army.

*Convalescence from prolonged illness and boarding cases to England.*—In peace time, most seriously ill Europeans were sent back to England to convalesce. It is not possible to do this now for lack of shipping space. We thus must reconsider what is the best disposal of men with such diseases as renal stone, bone tuberculosis, and medical diseases such as sprue, blackwater and resistant amœbiasis. Long convalescence in India is depressing, and it takes longer to get fit. Under Army conditions, renal calculi and sprue are likely to recur. We shall need to consider the effects on morale of large numbers of men in and out of hospital in a poor state of health in low categories. Finally, as the war goes into its fifth year, the Army in Eastern India will have to decide how long British troops will endure efficiently this damp hot climate, away from their families and often with few amenities for their health and happiness.

It has often been said here that this is a medical war. Medical officers have and will play a great part, not only in treating and preventing disease but in preserving and encourag-

ing the spirit of troops, and discounting their fears of ill health. We need to discuss these questions, to find out what men are thinking and feeling, to do our job well.

## Medical News

### THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed the D.T.M. Examination, session 1943-44.

*Passed*

(Arranged in alphabetical order)

1. Naresh Chandra Bagchi, L.M.F. (Bengal), Pathologist, Binnaguri Central Laboratory, Dooars.
2. Netai Pado Banerjee, L.M.F. (Patna), L.T.M. (Bengal), private practitioner.
3. Jagat Bandhu Basu, M.B. (Cal.), Air Port Health Officer, Dum Dum.
4. Mani Lal Basu, M.B. (Cal.), Medical Officer-in-Charge, Silver Jubilee Dispensary, Lillooah.
5. Pataki Charan Bhattacharjee, M.B. (Cal.), private practitioner.
6. Bishnu Pada Chaudhuri, M.B., D.P.H. (Cal.), private practitioner.
7. Chiang Tseng-Hsun, M.D. (National Medical College of Shanghai), Assistant Technical Expert, China.
8. Bimalapati Chowdry, M.B., B.S. (Lucknow), private practitioner.
9. Asoke Kumar Das, M.B. (Cal.), private practitioner.
10. Pashupati Das, M.B. (Cal.), private practitioner.
11. Asok Das Gupta, M.B., B.S. (Patna), private practitioner.
12. Satchida-nanda Ghosh, M.B., D.P.H. (Cal.), private practitioner.
13. Atulendu Goswami, M.B. (Cal.), private practitioner.
14. Syamalendu Goswami, M.B. (Cal.), private practitioner.
15. Tejendra Nath Guha Roy, L.M.F., L.T.M. (Bengal), Assistant Medical Officer, Mathura Tea Estate, Jalpaiguri.
16. Hari Prasad, M.B., B.S. (Patna), private practitioner.
17. Albert James Henderson, M.B., Ch.B. (New Zealand), Medical Officer, Jagadhri Mission Hospital, Punjab.
18. Shu-Wan Liu, M.D. (Peking Union Medical College), Medical Officer in China.
19. Haroon Haji Valli Lodhia, M.B., B.S. (Rangoon); private practitioner.
20. (Miss) Sheila Martin, M.B., B.S. (New Delhi), private practitioner.
21. (Miss) Rafia Mohsin Ali, M.B., B.S. (New Delhi), private practitioner.
22. Abani Mohan Nandy, L.M.F., L.T.M. (Bengal), Honorary Pathologist, S. K. Hospital, Mymensingh (awarded the 'Chuni Lal Bose Gold Medal' 1944).
23. Pan Shao-Chou, M.B., Hunan-Yale Medical College, Visiting Physician, Central Hospital, China.
24. Bibhuti Bhusan Pradhan, M.D. (Cal.), private practitioner.
25. Bimal Krishna Pramanik, L.M.F. (Bengal), Sub-Assistant Surgeon, Bengal & Assam Railway.
26. Sitanath Pramanik, M.B. (Cal.), private practitioner.
27. Saradindu Bhusan Sen Gupto, L.M.F. (Bengal), Senior Assistant Medical Officer, Dima Tea Estate, Dooars.
28. Keshab Lal Sen Sarma, L.M.F. (Bengal), Assistant Medical Officer, Gillapukri Tea Estate, Assam.

29. Gouri Shanker Sharma, L.M.F. (Central India), State Medical Officer, Jodhpur.
30. Mohan Lal Sharma, M.B., B.S. (Punjab), private practitioner.
31. Nathi Lal Sharma, M.B., B.S. (Lucknow), private practitioner.
32. Esther Gyanmoni Soule, L.S.M.F. (Agra), Medical Officer, Government Hospital for Women and Children, Egmore.

### PROGRESS OF HEALTH SURVEY COMMITTEE

Sir Joseph Bore, Chairman, Health Survey and Development Committee, in a broadcast from the All-India Radio on Monday, 10th April, said:—

The committee appointed by the Government of India to conduct a survey of the state of public health in the country and to make recommendations for the future has now been at work for about five months. It has been handicapped in the discharge of its task so far by the general conditions prevailing in the country. Suitable staff has been hard to find. Traveling conditions have not made it any easier to get witnesses and expert advisers to establish contact with members of the committee as and when required and so far as the essential touring, which still lies before the committee, is concerned, we can only hope that our plans will not be too severely dislocated by the impediments which in these days are inevitable.

In the country's reconstruction programme there has been some difference of opinion as to the priority to be given to the various lines of developmental progress. I would plead that the importance of health in the scheme of national life be prominently borne in mind in taking any decision as to its position in any priority list. There is hardly a single phase of national progress which is not vitally influenced by the health of the individual and the health of the community. I mean by this that the productive power of the individual and of the nation is conditioned by the efficiency with which minds and bodies function.

The connection between public health and public and national wealth is intimate and inseparable. The health and well being of the community is not an investment yielding deferred dividends. Its returns are immediate. How many million man-hours are lost every year in India to industrial establishments through absenteeism resulting from sickness? This is quite apart from the reduction of a worker's efficiency as the result of ill health and its debilitating consequences. If this loss could be eliminated or even reduced, the increase in the nation's production and wealth would be direct and immediate. I ask that this aspect of the importance and the urgency of health matters in any reconstruction programme should be prominently borne in mind.

#### *Time factor*

My committee recognizes the necessity for completing its investigations and making its recommendations as early as this is possible. The importance of the time factor is always before us but there is another factor which cannot possibly be ignored. Our investigations must be as complete and as thorough as the existing conditions permit. The field we have to cover is immense and if our proposals are not to be out of date before they see the light of day, having regard to developments elsewhere in the world, we must have time for examination and consideration.



The Goodenough Committee in the U.K. which is concerned with the task of reporting on medical education and research has already taken two years and its report has not as yet been published. Medical education and research are but a single facet of the problem which has been referred to us for consideration. Moreover, the Goodenough Committee is dealing with a more or less homogeneous population living under more or less similar conditions. In India the complexity of our problem is intensified a hundredfold by the diversity which faces us not merely between province and province but even between parts of a single province. Nevertheless, we will see to it and do our best to ensure that a reasonable balance is maintained between the time factor on the one hand and the necessity for ensuring that our report will not suffer unduly in quality and value because we have had perforce to work against time.

Touring in provinces is an essential part of our enquiry. Unfortunately it has had to be curtailed in extent and duration owing to existing difficulties of transport and accommodation. For the purpose of visits to the provinces the health committee has been formed into four groups, each constituted so as to represent all the five Advisory Committees into which the main committee has been divided. These groups will start on their tours almost at once and will carry on until about the end of May. Further touring may be called for but this will be decided later.

I would ask all those who feel that they can help our touring groups in the provinces with information and material of value to be so good as to get into touch with these groups and give them such assistance as they can. This will be deeply appreciated.

#### COW AND GATE MILK FOOD

We are glad to announce that Messrs. Cow and Gate Limited, Guildford, England, have donated a total of 200 cases of their milk food for the relief of distress in Bengal. The gift represents nearly 4,000 gallons of reconstituted milk.

#### BENZYL BENZOATE IN SCABIES

We have received from Messrs. May and Baker (India) Limited a descriptive booklet on the usefulness of a benzyl benzoate preparation in the treatment of scabies. Members of the medical profession who are interested in the subject may have copies of the booklet from the Company, Karimjee House, Sir Pheroze Shah Mehta Road, Bombay.

#### A HOSPITAL IN NEED

The hospital for sick children, Great Ormond Street, London, W.C.1, is Britain's oldest children's hospital. Over two million little ones have passed through its doors. Amid bombed ruins it is carrying on excellent work, but it is badly in need of funds. We have received a copy of an appeal for help, and those of our readers who are willing can send donations direct to Lord Southwood, Chairman of the hospital.

#### THE PHARMACEUTICAL AND ALLIED MANUFACTURERS' AND DISTRIBUTORS' ASSOCIATION, LIMITED

In the fourth annual general meeting of the Association held in Bombay in April 1944, the President, Mr. R. A. Haryott, referred to the Drug Control Order which had been so far, he thought, a success, and then stressed on the need for some relaxation of import restrictions whenever the shipping position should warrant it. Owing to Government appreciation of the need for increasing the supply of medicines, greater supplies had been forthcoming during the last

few months, especially from the United Kingdom. There was, however, a risk that there might be in the future even more acute shortages of medicines than there had been in the past, according to the effect upon the United Nations' shipping resources of the impending military operations on the Western Front. Whenever possible, he added, opportunities should be given to distributors to increase stock reserves by temporarily increasing their quotas to tide over future difficult periods.

#### SODIUM BISMUTH TARTARATE

(A DRUG FOR THE TREATMENT OF ARTHRITIS)

We have received from Messrs. C. J. Hewlett and Son, Limited, 35-43, Charlotte Road, London, a small leaflet giving details of 'SBT' brand sterilized solution of sodium bismuth tartarate which has been used for arthritis. A note on the results obtained from its use appeared in the *Lancet*, February 1944, page 264.

#### POST-WAR FOOD PLANNING\*

PLANS to take the British people off their pre-war diet of 'tea and margarine' and on to a diet of butter, milk and meat are being worked out for the Government by dietitians. This will involve the creation of a permanent food commission with wide powers to plan the production and distribution of health supporting foods for both rich and poor. Its work will include (1) reorganization of British agriculture to increase the production of milk; eggs, fruit, vegetables and meat, (2) distribution of these foods to secure a diet adequate for health within the reach of every family, however poor, and (3) organization of food either by home production or import, if necessary, to make certain that at no time will there be a shortage of any essential food.

Food experts who have advised the Government during the war are now planning for the post-war era. They hold that such a commission will revolutionize agriculture and lay the foundation of prosperity in other basic industries. White bread, margarine, jam and tea, regarded by large masses of people as a staple diet, will be discouraged. Instead, the people will be given an opportunity to increase their consumption of milk, eggs, fruit, vegetables and meat. World food policy, with which Great Britain will be closely linked, will be directed to the same end. The intention is now to extend the policy of 'enough to eat' to 'enough of the right kind of food'. Perhaps the most valuable dietetic reform to come from wartime food control was the abolition of white bread. The deficiency of vitamins and minerals produced in 'the staff of life, was one of the greatest evils of our civilization.

#### MEDICAL PROTOZOLOGY

The second edition of Knowles' 'Introduction to Medical Protozoology' has just appeared. It has been completely revised, abridged and re-written and brought up to date by Dr. B. M. Das Gupta, Professor of Medical Protozoology and Director of the Calcutta School of Tropical Medicine. This book will be reviewed in a future number of this journal. It has been recently very difficult or impossible to turn as a textbook on Medical Protozoology, and this book should meet an urgent need. Numerous new illustrations have been included and also several excellent coloured plates and the whole publication is a very creditable one. It is obtainable from the publishers, Messrs. U. N. Dhur and Sons, Limited, 15, Bankim Chatterjee Street, College Square, Calcutta. The price is Rs. 20/-.

\* Abstracted from the *Journal of American Medical Association*, 29th January, 1944, p. 316.



## Public Health Section

### DEGREE OF ACCURACY REALIZED IN MALARIA FORECASTS IN THE PUNJAB FOR THE YEARS 1923 TO 1942

By KHAN BAHADUR M. YACOB, M.B., B.S.,  
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and

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A METHOD for the forecasting of epidemic malaria was devised in the Punjab in 1921 by Gill (1928). In his studies on the relationship between the occurrence of localized malaria outbreaks and meteorological and other factors, he discovered certain close correlations and thus demonstrated that forecasts of epidemic malaria could be prepared from data relating to the following factors :—

- (i) the combined July and August rainfall,
- (ii) the spleen rate figures of selected representative localities as taken at the spleen census in June of each year,
- (iii) the epidemic potential factor, and
- (iv) the economic factor.

A brief discussion of these factors was set out by us in our previous paper (Yacob and Swaroop, 1944). Suffice it to state here that the combined conditions favourable to the occurrence of a severe malaria epidemic are—

- (a) a conspicuous excess of the July and August rainfall over the normal, or extensive floods,
- (b) a low spleen rate in the month of June,
- (c) relatively high epidemic potential factor, and
- (d) famine conditions or relatively high prices during the preceding year.

In that paper we analysed the records of the previous ten forecasts with a view to testing, from the statistical point of view, how far the previous predictions issued by the Punjab Public Health Department agreed with the actual happenings. Only those ten years were taken for this purpose for which the forecasts were prepared by one of us (M. Y.). The department has, however, been issuing the forecasts ever since 1921. In the present paper we discuss, from the statistical point of view, the degree of accuracy realized in the earlier attempts at forecasting, and compare the earlier forecasts with those issued relatively recently. In a general way, therefore, an assessment is made of the accuracy attained over the whole period.

The increased prevalence of epidemic malaria in the Punjab is confined to the autumn months of October to December each year. The forecasts for the years 1921 and 1922 were issued by Gill rather late in the malaria season, the forecast for 1921 was issued on the 29th September

and that for 1922 on the 16th September and as all the other forecasts have, under instructions from the Director of Public Health, had to be issued relatively much earlier we ignore these first two attempts at forecasting and confine ourselves to those issued for the succeeding twenty years, *viz*, from 1923 to 1942. Out of the forecasts for these twenty years the forecasts for ten years, *viz*, for the year 1929 and thereafter from 1934 onwards, were all issued by the same author (M. Y.). For the purpose of studying whether a personal factor has brought about any change in the forecasts, we divide the total experience of twenty years 1923 to 1942 into two periods; the first period to include all the earlier forecasts from 1923 to 1928 and again from 1930 to 1933, and the second period covering the forecasts for 1929 and thereafter from 1934 to 1942.

In 1922 Gill stated: 'I do not consider it expedient at present to attempt to give to these forecasts a precision to which they make no claim. I, therefore, prefer to use for the present at any rate more general terms such as "absence of epidemic malaria", "mild", "moderately severe", "severe epidemic conditions", rather than attempt to forecast the probable epidemic figures.' The wording of the forecasts issued by the department has throughout this period of 20 years contained these phrases, and although the meaning of these terms may be easily apprehended, their significance cannot be numerically assessed without introducing some element of arbitrariness. Since, however, we are more concerned with knowing whether in those localities in which epidemic conditions were predicted the epidemics did break out, we might, for the purpose of instituting statistical tests, compare the actual incidence or mortality of malaria in the two categories of districts, *viz*, (i) those in which according to the forecast an epidemic was anticipated and (ii) those in which no increased prevalence was considered likely.

Malaria cases are not notifiable either in the rural or the urban areas of the province, nor is the reporting of malaria deaths at all satisfactory in all the parts. We do not, therefore, have a completely reliable index of the incidence of malaria or its mortality. But it is a well-known fact that the disease reaches its highest incidence during the last quarter, and that the incidence of malaria is generally low in the second quarter of each year. If, therefore, it is known that there was no epidemic of influenza or relapsing fever, the deaths from which causes also are included under the omnibus heading 'fevers', an increased fever mortality in the latter half of a year or in the last quarter of a year can almost with certainty be ascribed to the prevalence of malaria.

An index termed 'epidemic figure' was accordingly employed by Gill to measure the actual

# HOWARDS'

## FINE CHEMICALS

BROMIDES

AETHERS

CITRATES

BISMUTHS

CINCHONAS

QUININES

IODIDES

MERCURIALS

SALICYLATES

THYMOL

TABLETS

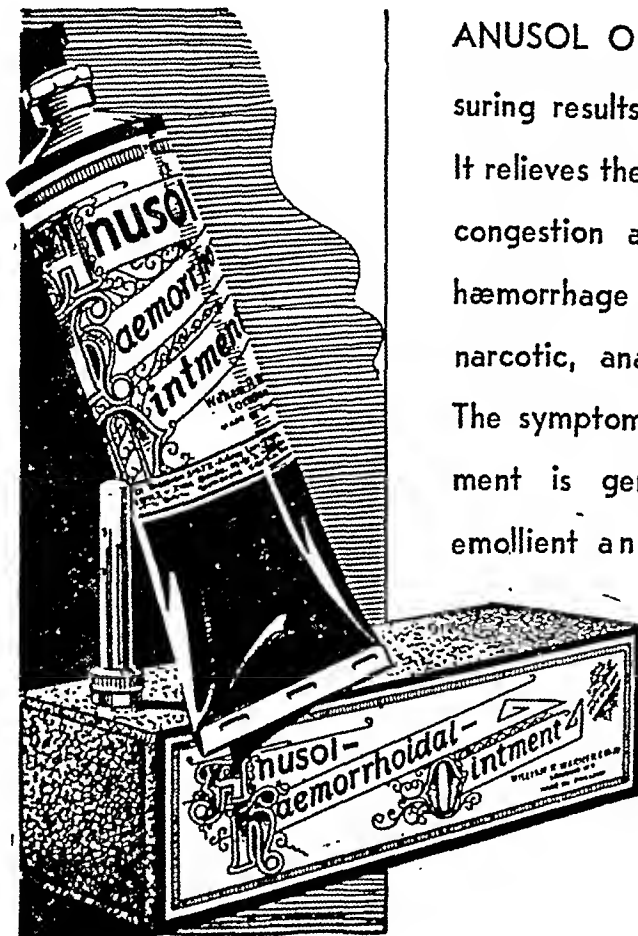
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incidence of malaria. This index is calculated by dividing the mean monthly mortality during the months of October to December by the mean monthly mortality of the previous months of April to July of the same year. The epidemic figure thus obtained indicates the ratio between the fever mortality during the malaria season and that during the non-malaria season of the same year. The value of this index in gauging the intensity of malaria in any locality or district is considerable. In normal years, i.e. the years when no epidemic of malaria occurs, this index has a value in the neighbourhood of 1.0. It generally increases in value in proportion to an increase in malaria, and under epidemic conditions may reach a figure as high as 10.0. Moderately severe epidemic conditions are reflected by an epidemic figure of about 2.5. It must be noted that the epidemic figure is calculated from death records only. If any place experiences an abnormal incidence of malaria characterized by only low fatality, as would normally happen in the case of outbreaks in endemic areas, such as Kangra, the epidemic figure would fail to provide a true record of the incidence of the disease. Thus, while a high epidemic figure would undoubtedly show that the locality did experience an epidemic, a low epidemic figure, on the other hand, would not be incompatible with the occurrence of an epidemic accompanied by low fatality. This point has to be specially borne in mind when examining the epidemic figures of places in which the occurrence of malaria had been predicted as against the epidemic figures of those places in which no epidemic was foreseen; for, if high incidence had been predicted and subsequently the epidemic figure turned out to be somewhat low, it would not necessarily imply that the prediction had gone entirely wrong. For the purpose of instituting statistical tests, however, the prevalence of malaria has been judged by the epidemic figure only without paying any regard to this possibility and, therefore, the statistical tests which have been carried out to assess the usefulness of the method of forecasting must be considered to be somewhat stringent on this account.

It must be stated that, in the forecasts, sometimes only certain isolated localities in different districts are mentioned as likely to experience epidemics of malaria. But since, in what follows, we have made comparisons of only the district figures, we have assumed for the purposes of statistical tests that the epidemic figures of the whole district in which this isolated locality was situated would show a relatively higher value. This, however, need not necessarily be true if the remaining part of the district remained almost entirely free. It is not unlikely that when the epidemic figure for the district as a whole is taken, no appreciable rise is noticed in this figure. It must, therefore, be noted, in the comparisons based on the figures for the district as a whole, that we are, on this account, also,

putting the accuracy of the forecast to a rather stringent test.

It was noted by Gill that prolonged conditions of humidity are highly conducive to the longevity of the insect carrier and thus give rise to increased prevalence of the disease. Such a humid climate is the natural outcome of the overflow of rivers or storm-water channels due to inundations. All districts so affected, therefore, should, other factors remaining the same, be expected to yield high epidemic figures. However, in the forecasts so far issued, the department was not able to know definitely in all cases the precise localities or districts affected by floods or prolonged collections of water and, therefore, at the time of preparing the forecast this factor had to be ignored. A perusal of the forecasts issued, *vide* Appendix II in which the forecasts for the year 1942 are quoted in full, would however show that usually it was so worded as to make a proviso that if any particular locality was affected by the overflow of rivers or inundations, epidemic conditions would occur. The names of the precise localities thus affected could not always be stated in the forecasts. In the absence of the information about inundated areas, the names of some districts which should normally have appeared in the forecast are left out. We shall, therefore, be imposing a more stringent test on the efficiency of the method of forecasting if we were to regard all such districts in which malaria epidemics occurred due to inundation but the names of which were not specifically included in the forecast as those in which the forecast did not, for the purpose of our statistical tests, come out to be true.

In Appendix I the epidemic figures of all the districts are given for each of the twenty years 1923 to 1942. Appendix II shows for the year 1942 the forecasts that were issued. Two forecasts are issued each year, *viz.* (i) preliminary, usually issued towards the end of August, and (ii) the final forecast based on complete data up to the end of August of each year. This is issued by the end of the second week of September. It has sometimes happened that for some unforeseen reason the rainfall data or other relevant data could not become available to the department from some districts by the time the forecast had to be issued. In such cases no statement is, or can be, made of the likelihood of epidemic outbreaks. The number of such districts is not large. In our previous paper we were able to leave out from consideration all those districts for which complete data had not been received in the department before the issue of the forecast. In the case of the earlier years, however, no information is available about such districts. Thus while districts about which no mention is made in the forecast might have experienced an increased prevalence of malaria and should have legitimately been included in that group of districts in which epidemic malaria was predicted, we have no other alternative but to classify these districts along with those

in which epidemic was not considered likely. This adds another element of stringency to statistical tests carried out later in this paper.

The epidemic figures of those districts which were considered in the annual forecasts (preliminary and final) to be likely to experience epidemics of malaria are marked with asterisk signs in Appendix I. For any one year the districts in the Punjab can thus be classified into two groups:

(i) Those marked with an asterisk and in which an epidemic of malaria was predicted.

(ii) Those free from the asterisk sign and for which no mention was made in the forecasts about the likelihood of an increase in incidence.

The average values of the epidemic figures of the districts falling in each of these two groups have been separately calculated and by means of the usual Fisher's 't' test the statistical significance of the difference between the two means has been tested. In the table I, the two means, their differences, the standard errors of the differences and other relevant figures are set out, and in the last column the statistical significance has been assessed. Similar data for the remaining ten years were set out in table III of our previous paper.

this year must be regarded as entirely wrong. However, the difference is only - 0.0121 and is only a fraction of its standard error of 0.0988 and is consequently not to be considered significant. From the second column of table I, in which the mean epidemic figure for the whole province is given, it would appear that the province can be considered to have experienced malaria epidemics only during the four years, *viz*, 1924, 1925, 1926 and 1933. For the first three of these four years the forecasts proved significantly successful as judged statistically.

There is yet another purely theoretical consideration which increases the stringency of the 't' tests carried out between the means of the epidemic figures of districts in which malaria was predicted as against that of the districts in which no epidemic was considered likely. The amount of error by which to judge whether the difference between the two mean epidemic figures is significant or not is based on the degree of variation that the epidemic figures of the individual districts separately show round the two respective means. The assumption that is implicit in this calculation is that the epidemic figures of the individual districts in each group all belong to one homogeneous population having

TABLE I

Year	Mean epidemic figure of			Difference between columns (3) and (4)	Standard error of the difference in column (5)	Statistical significance of the difference in column (5)
	the whole province	the districts in which malaria was predicted	the districts in which malaria was not predicted			
(1)	(2)	(3)	(4)	(5)	(6)	(7)
1923	1.3	1.3213	1.3017	0.0142	0.1432	Insignificant.
1924	1.5	1.9366	1.3480	0.5886	0.2453	Significant.
1925	1.5	1.7977	1.2394	0.5583	0.2266	Do.
1926	1.9	2.3910	1.6942	0.6968	0.2677	Do.
1927	1.0	1.2957	0.8991	0.3966	0.1048	Do.
1928	0.9	1.0700	0.9104	0.1596	0.1684	Insignificant.
1930	1.2	1.2740	1.2216	0.0524	0.0735	Do.
1931	1.4	1.4282	1.3292	0.0990	0.1297	Do.
1932	1.3	1.3025	1.3146	-0.0121	0.0988	Do.
1933	2.2	2.2339	2.0536	0.1803	0.3722	Do.

The difference between the mean of the epidemic figures of districts in which malaria was predicted is in significant excess of the mean of the districts falling in the other category for each of the years 1924, 1925, 1926 and 1927. In the case of remaining years the limit of statistical significance is not reached. It must be noted that of these remaining years, the deviations are for five years in favour of the method of forecasting, but one year, *viz*, 1932, stands out in marked contrast, as the mean epidemic figure for districts in which malaria was predicted happened to be lower than the mean of those districts in which malaria epidemics were not foreseen. The forecast for

the same mean, and that the variation between the individual epidemic figures is wholly due to chance. This would be a legitimate assumption if we could expect all districts in any of the two groups, *viz*, in which malaria was predicted or those in which epidemic was not predicted, to show similar epidemic figures. But we know that for that group in which districts with the likelihood of epidemics fall, the epidemic figure may have widely varying values, and the total amount of this variation cannot wholly be a chance occurrence. If, therefore, we use this variation to form an estimate of an error due purely to random causes, we are detracting considerably from the precision of our test and



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even if the two means should in reality show significantly different values, the estimate of error so obtained is likely to considerably mask this significance. Thus, while the significant results already established have, on this account, their significance further confirmed, we must take note of this additional stringency of the statistical test in interpreting the significance for the remaining years. One way of making allowance for this enhanced variance might seem to be to base the calculation of error on only those series of epidemic figures which relate to districts in which malaria was not predicted. In doing so, however, we shall again be losing precision, for the number of degrees of freedom on which the test will be based will be considerably reduced and, further, it would indirectly imply our taking for granted in advance that the forecasting method was successful—a hypothesis which is what we are testing.

What is the statistical significance of the success attained during all these ten years considered together? We must examine whether, taken collectively, the mean epidemic figure of the districts in which malaria was predicted was greater or not than the mean of the districts in which malaria outbreaks were not considered likely. The different years show considerable variation in respect of epidemic prevalence, and in discussing the differences between the two types of districts we must eliminate the annual variation from the comparison. Two methods of treatment are available:—

(i) We may consider only the annual differences between the means of the two classes of districts. These are given in column 5 of table I. The average value of these ten differences is  $+0.2734$  accompanied by a standard error of  $0.0833$ . The value of Fisher's 't' for the 9 degrees of freedom is  $3.28$  and shows that the mean difference is statistically significantly different from zero. It thus demonstrates that the method has been successful in forecasting when the experience of all the ten years is considered together.

(ii) Analysis of variance of the two series of figures in columns 3 and 4 may be worked out on the same lines as explained in our previous paper. The total variability exhibited by these twenty mean epidemic figures can be ascribed to the following causes:—

(i) due to variation from year to year.

(ii) due to the variation between the two types of districts, and

(iii) due to the interaction between years and the two types of districts. Table II summarizes the results of this analysis of variance.

The 'between district' variance is more than ten times the variance due to interaction. If we make the usual assumption that the mean variance due to the interaction of districts and years is due primarily to random causes, we are led to the conclusion that the 'between district' variance is statistically significantly different from what might be expected from pure

TABLE II

Source of variation	Degrees of freedom	Sum of squares	Mean variance
Between the two types of districts.	1	0.3736	0.3736
Between years	9	2.5818	0.2869
Interaction	9	0.3123	0.0347
TOTAL ..	19	3.2677	..

chance and, therefore, the significant success of the method of forecasting is established over the whole period of ten years for which the records have been studied. It was explained in our previous paper that another estimate of error with which to compare the between-district variance of  $0.3736$  can be obtained from the consideration that each of the means in columns (3) and (4) of table I arises from a series of epidemic figures of individual districts, and the variability which those figures show round their respective means may be utilized for forming an estimate of the error; the advantage being that such an estimate will be based on a larger number of degrees of freedom. This variability cannot, as has already been remarked, be wholly considered as due to random causes and, therefore, this comparison would at the same time seem to make the test more stringent against the method.

In table III the variability of the individual epidemic figures round their respective means and between means has been analysed.

TABLE III

Source of variation	Degrees of freedom	Sum of squares	Mean variance	Adjusted mean variance comparable to the variances of Table II
Between means.	19	57.3719	..	...
Within means.	270	61.6817	0.22845	0.0221
Total ..	289	119.0536	..	..

In the last column of this table, the 'within-means' variance has been suitably weighted, as explained in our previous paper, to make it comparable to the variances set out in table II. The between-district variance of table II is now seventeen times the error variance of  $0.0221$ , and this comparison further confirms the significance of the success of the method of forecasting over the ten years judged collectively.

A further extension of the analysis of variance enables us to study whether the accuracy in forecasting has changed from the first ten-year group (1923 to 1933 with the exclusion of 1929) to the next group of ten years (1929 and 1934 onwards) and also whether judged collectively over the whole period of these twenty years, the forecasts were successful. In the following table the mean epidemic figures of the two types of districts in each of the two groups of periods are set out :—

variance should ordinarily be associated with 19 degrees of freedom, but, as has been shown in what follows, one degree of freedom is absorbed in the comparison between the two periods; we are left with only 18 degrees of freedom for this variance. It may be stated that the variability within years is judged round the respective means of the two periods.

(iii) Between the two periods. The variation that might exist in the two mean epidemic figures of the two periods is taken care of by

TABLE IV

Years	FIRST GROUP OF YEARS		Years	SECOND GROUP OF YEARS	
	Mean epidemic figure of			Mean epidemic figure of	
	the districts in which malaria was predicted	the districts in which malaria was not predicted		the districts in which malaria was predicted	the districts in which malaria was not predicted
1923	1.3213	1.3071	1929	2.3085	1.1720
1924	1.9366	1.3480	1934	1.3756	1.0645
1925	1.7977	1.2394	1935	1.1242	1.0230
1926	2.3910	1.6942	1936	1.0020	1.0340
1927	1.2957	0.8991	1937	1.7650	0.9781
1928	1.0700	0.9104	1938	1.0470	0.8057
1930	1.2740	1.2216	1939	1.0600	0.9922
1931	1.4282	1.3292	1940	1.3784	1.1356
1932	1.3025	1.3146	1941	1.3356	1.3191
1933	2.2339	2.0536	1942	2.7618	1.6078

An analysis of the total variability of these forty mean epidemic figures may be carried out as follows :—

(i) Between the two types of districts. In this case we suppress all the other variables, *e.g.* the years and the two periods, and make a comparison of the grand mean of the epidemic figures of districts in which malaria epidemics were predicted with the mean of the epidemic figure of all those districts in which no such occurrences could be foreseen. If the variance from this cause can be shown to have a significantly higher value than the variance arising from random causes alone, it would demonstrate that the method of forecasting showed accuracy to a statistically significant degree when judged over the whole range of twenty years, after making allowance for the variability due to different degrees of prevalence of disease in different years as well as for the differences that might be found in the two ten-year periods. This variance will be associated with only one degree of freedom.

(ii) Between years. A significant value of this will only demonstrate the differences existing between the different years in respect of the epidemic conditions. However, an evaluation of the variance due to this cause is essential, as we must make allowance for this variability in other statistical comparison such as that between the means of the two types of districts. This

the variance which is based on one degree of freedom.

(iv) Interaction between the two periods and the two types of districts. The variance corresponding to this interaction possesses a relevant interpretation, for if it can be shown that this variance is greater than can be expected from chance alone, we can state definitely that within the two periods the success of the method underwent a significant change in the degree of accuracy. The estimate of the variance will be based on one degree of freedom.

(v) Interaction between years and the two types of districts. In the absence of any better estimate, the variance due to this interaction may legitimately be considered to provide an estimate of the error due to random causes.

A summary of the results of the analysis of variance carried out on these lines is presented in table V.

The 'between district' variance is sixteen times the error variance of 0.0701, and from a statistical point of view is significantly higher than the latter. It is, therefore, statistically established that over the whole period of twenty years the method of forecasting has yielded a statistically significant success.

The variance due to the interaction between the two periods and the two types of districts is low, and indicates that between the two ten-year periods no relative change occurred in



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# APPENDIX I

Epidemic figure for each year and district. Asterisk marks against a district indicate that in the forecast an epidemic of malaria was predicted in that district. Figures enclosed in brackets relate to districts for which the basic data for formulating forecast had not been received by the time the forecast was issued.

District	Years																			
	1923	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942
Hissar	* 1.47	0.78	* 1.26	* 2.60	* 0.94	0.64	1.03	* 1.25	* 1.25	0.91	* 1.45	1.03	* 1.03	0.64	0.79	0.59	0.63	1.08	1.07	* 5.71
Rohtak	1.42	0.86	* 3.23	* 2.25	* 0.76	0.64	0.91	0.93	* 1.19	0.90	1.89	1.29	* 1.08	* 0.86	0.97	0.82	1.08	* 0.84	0.80	* 4.16
Gurgaon	1.19	1.29	* 2.35	* 2.35	* 1.36	0.54	0.92	* 1.32	* 1.41	* 0.87	1.90	* 1.45	* 1.32	* 1.27	0.72	0.87	0.87	* 1.14	0.74	(4.21)
Karnal	2.01	1.05	* 2.68	* 1.37	0.83	0.61	0.87	1.63	1.39	* 1.47	* 1.70	* 1.12	* 1.69	0.77	0.96	0.51	1.51	1.08	0.99	* 5.45
Ambala	2.24	1.82	* 2.25	* 2.04	* 1.44	0.76	0.88	* 1.22	* 1.69	* 1.43	* 2.27	* 0.93	1.18	* 0.96	0.99	0.91	2.13	* 1.13	* 0.96	* 3.94
Simla	1.64	0.72	0.14	1.50	0.62	0.16	1.33	0.96	0.57	1.48	1.14	0.42	0.88	0.80	0.88	0.88	0.53	0.72	0.56	0.69
Kangra	1.15	1.09	1.05	1.51	0.96	1.02	1.17	1.04	* 1.01	1.13	1.09	1.05	0.84	0.93	* 1.12	* 0.88	* 1.11	* 1.08	* 1.21	* 1.28
Hoshiarpur	1.32	1.39	1.56	2.34	* 1.13	0.90	1.33	1.21	* 1.11	* 1.39	1.39	1.03	* 0.89	* 0.96	0.91	0.81	0.78	* 1.37	* 1.06	1.60
Jullundur	* 1.36	1.20	* 1.51	* 2.55	0.99	* 1.05	1.19	1.06	* 1.14	* 1.38	* 1.23	1.14	* 0.96	* 0.93	0.86	0.86	0.85	* 1.11	1.02	1.61
Ludhiana	* 1.54	1.32	* 1.85	* 2.00	0.77	0.93	1.10	1.22	* 0.95	* 1.41	1.49	0.87	* 0.92	* 1.07	0.92	(0.92)	0.96	* 1.39	1.12	* 3.07
Ferozepore	* 1.42	1.16	* 1.09	1.42	0.68	0.80	1.22	* 1.13	* 1.68	* 1.20	* 1.73	* 1.10	* 0.99	* 1.11	1.09	0.88	1.02	* 1.09	1.63	* 3.22
Lahore	1.54	* 1.51	* 1.33	1.92	0.80	0.89	* 1.30	* 1.13	* 1.63	1.11	* 1.12	1.07	0.82	* 0.85	0.75	0.70	0.87	0.99	1.00	* 2.92
Gurdaspur	1.47	* 1.51	* 1.60	* 2.94	1.03	1.15	1.18	* 1.13	* 1.68	1.19	* 1.31	1.08	* 0.87	* 0.87	0.93	0.69	0.92	* 0.98	1.58	* 0.93
Amritsar	1.74	* 3.15	* 2.41	3.38	* 1.56	1.13	* 1.36	* 1.40	* 1.83	1.43	* 2.27	1.30	* 1.18	* 1.16	1.05	0.90	0.92	* 1.89	1.53	(2.59)
Sialkot	* 1.39	* 2.86	2.43	3.98	* 1.38	1.24	1.26	1.09	* 1.91	1.59	* 2.97	* 1.52	* 1.20	* 1.07	0.97	0.89	0.89	* 1.83	1.33	2.16
Gujranwala	* 0.97	2.03	2.00	2.24	0.87	0.99	1.03	1.34	* 2.16	1.26	* 4.84	* 1.77	* 1.41	0.88	1.04	0.74	1.07	* 1.53	2.06	(2.27)
Sheikhpura	1.23	2.05	1.46	1.96	0.81	0.98	1.26	1.12	1.72	1.24	* 2.79	1.25	* 0.99	* 0.88	0.93	0.70	0.92	1.57	1.90	* 2.10
Gujrat	1.23	* 3.19	1.81	2.59	1.15	1.06	* 1.69	1.22	1.50	1.39	* 3.81	* 1.77	1.15	* 0.86	1.04	0.92	1.05	* 1.66	1.44	* 3.52
Shalpur	0.75	1.52	0.90	1.26	0.63	0.93	* 2.53	1.07	1.05	* 1.17	* 2.73	* 1.16	0.77	0.75	0.73	(0.41)	0.75	0.97	* 1.48	* 1.94
Jhelum	1.28	* 1.54	1.15	2.47	1.08	1.22	* 2.59	1.30	1.61	1.47	* 2.72	1.44	* 1.14	1.00	1.22	1.00	1.06	* 1.66	* 1.82	* 2.21
Rawalpindi	1.33	1.39	1.26	* 1.82	1.19	1.11	* 1.80	1.31	1.46	1.59	* 2.13	1.53	* 1.47	* 1.18	* 2.41	* 1.37	1.13	* 1.30	* 1.86	1.26
Attock	1.17	1.35	1.11	2.00	1.14	1.07	* 2.32	1.35	1.45	1.84	* 2.42	* 1.56	* 1.26	1.10	1.01	(1.29)	* 1.01	* 1.91	1.60	1.97
Mianwali	0.91	2.49	0.88	1.04	0.79	1.04	* 2.95	1.40	1.39	* 1.60	2.18	0.92	* 1.23	1.35	1.08	0.87	1.02	1.30	1.41	* 2.05
Montgomery	* 1.42	* 1.20	* 1.01	1.14	0.74	0.98	1.89	* 1.60	* 1.51	* 1.20	* 1.69	1.14	* 0.94	1.11	1.06	0.74	1.02	* 1.20	1.25	2.27
Lyalpur	* 1.00	* 0.98	* 1.09	1.12	0.70	1.02	* 1.22	* 0.89	* 1.04	* 0.95	* 1.04	1.11	* 0.79	0.79	0.81	0.56	0.80	0.91	1.03	* 1.41
Jhang	1.08	1.39	1.02	1.10	0.82	0.89	* 2.31	1.27	0.99	* 0.92	2.33	0.67	0.97	1.08	0.91	0.63	0.66	(1.41)	1.95	1.30
Multan	1.11	1.27	1.03	1.13	0.76	0.78	* 2.10	1.26	* 1.09	* 1.13	3.44	0.89	1.07	1.39	1.07	0.82	0.96	* 1.22	1.65	1.56
Muzaffargarh	0.93	* 1.49	1.08	1.01	1.00	0.98	* 3.34	1.52	1.39	* 1.77	3.40	1.02	1.42	1.88	1.28	0.91	1.26	1.60	1.59	* 1.78
D. G. Khan	0.71	0.79	0.90	1.06	0.98	1.20	* 4.75	1.22	1.43	* 1.52	3.34	1.04	1.13	1.78	1.44	1.22	1.12	* 1.86	1.30	2.21



TABLE V

Source of variation	Degrees of freedom	Sum of squares	Mean square
Between the two classes of districts (malaria predicted vs. malaria not predicted).	1	1.1255	1.1255
Between the two 10-year periods.	1	0.2292	0.2292
Interaction between the two 10-year periods and the two types of districts.	1	0.0386	0.0386
Between years ..	18	5.2216	0.2901
Interaction between years and the two types of districts.	18	1.2609	0.0701
Total ..	39	7.8758	..

so far as the degree of accuracy was concerned. In other words, the method has had some consistency, tending neither towards improvement nor towards increasing degree of failures. This interaction fails to emerge into significance even if we revise our estimate of error by considering, as might legitimately be done, the variability of each individual district epidemic figure round the mean of its own group and by adequate weighting as was done for carrying out the comparisons in table III. It is needless to set out the calculations regarding this revised estimate of error, as no new significance is established. Suffice it to state that this revision brings down the estimate of error to about one half of the previous figure of 0.0701, and only serves to confirm our previous results that during the period of twenty years—

(i) the method of forecasting has been significantly successful, and

(ii) between the two ten-year periods described earlier there has been no material change in the degree of accuracy attained in forecasting.

#### Summary and conclusions

Ever since 1922 the Punjab Public Health Department has been issuing each year preliminary and final forecasts of the probable occurrence of malaria in specified localities sufficiently in advance of the onset of the malaria season. A critical study has been made, from the statistical point of view, of the degree of accuracy attained in these forecasts. Although the statistical tests employed have been unavoidably stringent against the efficacy of the method of forecasting, yet, over the whole period of twenty years, viz, from 1923 to 1942, it has been established that the method enabled the officers of the department to specify in advance the localities where epidemic conditions subsequently developed. The experience of the twenty years has also been studied separately in two groups of ten years each. While in each of these two periods also the usefulness of the method has been statistically established, there is no indication that the method has undergone

any change in the degree of accuracy in the more recent years. It is now suggested that, on the basis of this accumulated experience of twenty years, the application of modern methods of statistical analysis should provide an improved and objective method of forecasting epidemic malaria.

#### Acknowledgment

The assistance rendered by Mr. Kartar Singh of the office of the Director of Public Health, Punjab, in compilation work is gratefully acknowledged.

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#### APPENDIX II

*Preliminary malaria forecast, issued on 28th August, 1942*

A study of the available July–August rainfall data up to 24th August and other forecasting factors indicates that owing to heavy monsoon rainfall and subsequent floods in various rivers and storm-water channels epidemic conditions are likely to develop throughout the major portion of the plains of the Punjab during the ensuing autumn. The areas likely to be affected are as follows:—

1. Hansi, Bhiwani, Budhlada and Tohana in Hissar district.
2. Rohtak, Gohana, Sallawas and Sonapat in Rohtak district.
3. Panipat, Karnal, Rajaund, Kaithal and Thaneswar in Karnal district.
4. Jagadhri, Ambala, Naraingarh, Kharar and Rupar in Ambala district.
5. The environs of Ludhiana town and the areas flooded by the Budha Nullah and the Sutlej river in Bet Ilaga of Ludhiana district.
6. Moga, Zira, Ferozepore, Nathana and the thanas of Makhu, Mallanwala, Guru Harsahai affected by floods from the Sutlej river and the Sukar Nullah in Ferozepore district.
7. The environs of Lahore town, Kasur and parts tehsil Lahore, tehsil Chunian and tehsil Kasur affected by floods in the rivers Ravi and Sutlej in Lahore district.
8. Tarn Taran, Ajnala and the areas flooded by the Ravi, Sukki and Hansli Nullahs in Amritsar district.
9. The environs of Gujrat town and parts of Gujrat tehsil affected by floods from the river Chenab in Gujrat district.
10. Bebra in Shahpur district.
11. Chakwal in Jhelum district.
12. Riverain tracts near Daud Khel and the western boundary of Mianwali district affected by extensive floods in the Indus.
13. Toba Tek Singh in Lyallpur district.
14. Low-lying riverain tracts affected by floods in the Indus and Chenab rivers in Muzaffargarh district.

In addition to the above epidemic nuclei of considerable intensity are likely to develop in:—

- (i) the Bajawat Ilaga of Sialkot district affected by floods from the Ravi and the Chenab and the areas affected by over-flowing water from the Basater, Aik and Deg Nullahs.
- (ii) areas affected by severe floods in Sidhanwali, Shahdara, Sharakpur, Baraghar and Syedwala thanas in Sheikhupura district.

Moderately severe epidemic conditions are also likely to affect parts of Nurpur and Dehra tehsils in Kangra district.



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The final forecast based on an analysis of the complete provincial data up to 31st August will be issued on 15th September, 1942.

*Final malaria forecast, issued on 13th September, 1942*

A study\* of the forecasting data for the whole province including rainfall recorded up to 31st August confirms the preliminary forecast issued on the 28th

August in all material respects. In amplifications of the prediction then made it may be stated that a widespread regional epidemic of malaria of considerable intensity is likely to visit all districts in the plains of the Punjab in which the July-August rainfall has been above normal. Epidemic conditions are likely to be particularly severe in areas which have been flooded by overflow water from rivers and storm-water channels.

## Current Topics

### Cold Hæmagglutinins in Acute Hæmolytic Reactions

#### in Association with Sulphonamide Medication and Infection

By W. DAMESHEK, M.D.

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIII, 11th September, 1943, p. 77)

SEVERE hæmolytic reactions occurred in 3 cases of acute infectious disease in which sulphadiazine and sulphathiazole had been used. They were associated with the presence in the blood of potent cold hæmagglutinins, which were also active against the patient's own red blood cells (autoagglutinin). In 2 cases, so-called virus pneumonia was present; in the third, a case of infectious mononucleosis, potent heterophile sheep cell agglutinins were also found. It is probable that both the drug and the hæmagglutinins were casually related to the sudden development of intravascular hæmolysis with hæmoglobinuria and acute hæmolytic anæmia. Recognition of the presence of a cold hæmagglutinin is important both diagnostically and therapeutically, especially from the standpoint of possible transfusions. Chilling of the patient with 'virus' pneumonia should be avoided.

### Thyrototoxicosis Treated with Thiourea

By H. P. HIMSWORTH, M.D., F.R.C.P.

(Abstracted from the *Lancet*, ii, 16th October, 1943, p. 465)

THE purposes of this paper is to report the full confirmation of Astwood's claims for the initial effects of thiourea on cases of thyrototoxicosis. Six cases have been treated, but it will suffice to report the effect of the therapy on one of the most severe.

#### MODE OF ACTION OF THIOUREA

The discovery of the action of thiourea on the thyroid gland was unexpected and for that reason the more credit is due to its discoverers for their alertness and the promptness with which they recognized the significance of their observations. J. B. and C. G. Mackenzie and McCollum were studying the effect of sulphaguanidine as an intestinal disinfectant and came to investigate its toxicity to the rat. They noted that animals dying after sulphaguanidine showed goitres and that on section the thyroid tissue showed hyperplasia and loss of colloid. This work was soon confirmed and it was further shown that other sulphur compounds, notably thiourea and thiouracil, had a well-marked goitrogenic effect. By a curious coincidence another group of workers arrived at the same conclusion from an entirely different starting-point. Kennedy and his colleagues in New Zealand were investigating the action of rape seed in producing goitre, and Kennedy was led to try the effect of allyl-thiourea. He discovered that it was actively goitrogenic. Since these discoveries, work to elucidate the mode of action of these thio compounds has been actively pressed forward. The results of these investigations have now

been published and throw considerable light on the matter.

When thiourea is given to rats two groups of effects are found: hypothyroidism and goitre. Clinically the animals show evidence of hypothyroidism by a falling basal metabolic rate, decreased growth and development, and a reduced appetite. Histologically the enlarged thyroid glands show hyperplasia and lack of colloid and resemble tissue from human cases of thyrotoxicosis. The classical work of Marine, however, has shown that this histological picture does not necessarily indicate thyrotoxicosis; rather it should be interpreted, in the normal animal at least, as meaning that the thyroid gland is producing insufficient of the thyroid hormone for the needs of the body and is being stimulated to hyperplasia to remedy the deficiency. For example, Marine showed that such hyperplastic glands occurred in animals on an iodine-deficient diet and that their histological picture reverted towards normal when iodine was given. The explanation put forward is that on the deficient diet the tissues suffered from lack of the iodine-containing hormone; normally such a state is corrected through the agency of the thyrotropic hormone of the anterior pituitary gland which stimulates the thyroid gland to become hyperplastic and more active. But even a hyperplastic thyroid cannot manufacture the thyroid hormone without iodine, and so the stimulus continues and the hyperplasia intensified. When under such conditions iodine is given, the thyroid hormone is produced in quantity, the stimulus to hyperplasia of the thyroid abates and the gland reverts to its 'resting' state.

It can easily be seen that the clinical state of hypothyroidism in association with a hyperplastic thyroid gland, such as occurs after administration of thiourea to normal rats, could be explained on the basis that thiourea neutralized the action of thyroxine in the body tissues. But such an explanation is immediately disproved by the observation that thyroxine has a normal action in animals under the influence of thiourea. It has also been shown that the condition of thyroid hyperplasia following administration of thiourea differs from the hyperplasia of iodine deficiency in that administration of iodine does not result in its disappearance and a return of the gland to the resting state. The question now arises: Is the hyperplasia of the thyroid tissues following treatment with thiourea mediated, as are other experimental thyroid hyperplasias, by the anterior pituitary gland? That this is the case is shown by the fact that hyperplasia after thiourea does not occur in hypophysectomized animals. It appears, therefore, that excessive secretion of thyrotropic hormones of the anterior pituitary gland occurs in animals treated with thiourea. We know, however, that when thyrotropic hormone is injected into normal animals it not only produces hyperplasia of the thyroid but also the condition of hyperthyroidism. The problem is why the hyperplasia after thiourea, which is apparently brought about by the agency of the thyrotropic hormone, is associated with hypothyroidism? The answer is given by the observation that thiourea prevents the development of hyperthyroidism which normally follows injection of this hormone while not preventing the hyperplastic effect of the thyrotropic hormone on the thyroid gland. The

suggestion follows that thiourea prevents the synthesis of the thyroid hormone. Experimental evidence supporting this view has recently been produced by Geish, who has shown that the colloid in the thyroid glands of animals treated with thiourea differs from normal thyroid colloid in being devoid of iodine.

These considerations provide theoretical grounds for suggesting the ultimate effect of treatment with thiourea. Marine has shown that hyperplasia of the thyroid gland, if unrelieved, ultimately gives way to atrophy with consequent hypothyroidism. It is possible therefore that long-continued administration of thiourea to human cases of thyrotoxicosis, in that it does not tend to diminish the hyperplasia but on the contrary has theoretical possibilities of intensifying it, may tide the patient over until atrophy of the gland supervenes and the state of thyrotoxicosis is thus cured by destruction of the source of the thyroid hormone.

#### SUMMARY

The claims of Astwood regarding the strikingly beneficial effect of thiourea on cases of thyrotoxicosis have been confirmed in six cases, so far as the initial effect of the drug is concerned.

The evidence at present available indicates that thiourea acts by interfering with the synthesis of the thyroid hormone.

### The Therapeutic Action of Penicillin on *Spirochaeta recurrentis* and *Spirillum minus* in Mice

By E. M. LOURIE

and

H. O. J. COLLIER

(Abstracted from the *Annals of Tropical Medicine and Parasitology*, Vol. XXXVII, 31st December, 1943, p. 200)

1. RELAPSING fever is sometimes, especially in tick-transmitted forms, stubbornly resistant to treatment by the arsenobenzene derivatives (e.g. Adler, Theodor and Schieber, 1937; Francis, 1938). Indeed, the disease (apparently a louse-borne variety) has even been known to arise actually during a course of anti-syphilitic treatment by one of these compounds (Johnson, 1925). There is accordingly a need for alternative means of drug treatment, and special merits have been claimed for preparations of bismuth (e.g. Todd, 1930) and gold (e.g. Steiner and Fischl, 1929). The experiments recorded in the present paper not only show that penicillin is active against experimental infections with the causative spirochete, but they suggest that it may even be considerably more effective than neoarsphenamine, which has been authoritatively singled out as the best drug in the treatment of this disease (Manson-Bahr, 1940). It need hardly be emphasized that the claims upon existing supplies of penicillin, either for trial or for more extended application, are far more pressing in other conditions than in relapsing fever.

2. The potential superiority of penicillin over neoarsphenamine is even more strongly suggested in the results which we have obtained in infections with the causative agent of rat-bite fever. There is, however, less need of new remedies for this disease than for relapsing fever, because of its very much lower and more sporadic incidence, and its more regularly dependable response to currently used drugs.

3. Since both these spirochaetoses in man are, on the whole, eminently amenable to treatment by standard anti-syphilitic arsenicals, and since they have proved in our experimental infections to be susceptible also to penicillin, the question naturally arises whether penicillin may not be effective against syphilis.

4. Penicillin was found to have no action against experimental infections with *Trypanosoma rhodesiense*, *T. congolense*, *T. cruzi* and *Plasmodium relictum*.

### The Extra-Erythrocytic Origin of Gametocytes of *Plasmodium gallinaceum* Brumpt, 1935

By S. ADLER

and

I. TCHERNOMORETZ

(Abstracted from the *Annals of Tropical Medicine and Parasitology*, Vol. XXXVII, 31st December, 1943, p. 148)

#### SUMMARY AND CONCLUSIONS

BIRDS were inoculated with *Plasmodium gallinaceum* by the bites of infected mosquitoes, *Aedes aegypti*.

Quinine (150 mgm. per kilo body-weight) was injected, in some cases immediately after the inoculation, in others three days later, and injections were continued daily in order to eliminate erythrocytic schizogony.

The injections were stopped when a sufficient infection with small non-pigmented parasites was established in red cells, and the subsequent development of the blood infection was studied.

Some merozoites derived directly from extra-erythrocytic forms invade red cells and develop directly into gametocytes.

#### Blood Urea

By REV. R. M. BARTON, M.A. (Oxon.)

(From the *Journal of the Christian Medical Association of India, Burma and Ceylon*, Vol. XIX, March 1944, p. 54)

THE following short paper has been written in response to requests from the Editor and a number of others, for details of a simple method of blood urea estimation, which can be used in a small hospital by the ordinary laboratory technician. Some description of the source of urea in the blood and the significance of increased findings have been added, as they may perhaps be of general interest to a number of readers of the journal.

#### ORIGIN OF UREA IN THE BLOOD

Proteins, which form one of the main food groups, are found mainly in animal food such as meat, fish, milk and eggs, and also to a lesser degree in certain cereals, vegetables and fruits. The digestion of these begins in the stomach, where pepsin and hydrochloric acid together begin the process of converting them into simpler substances called peptones, an intermediate stage in the process being called proteoses. Peptones, however, are still too complex to be absorbed by the body, and therefore in the small intestines they are further broken down. Trypsinogen, one of the enzymes of the pancreatic juice, converts them into amino-acids, which are simple enough to be absorbed into the blood stream. Here they are used partly to provide cells with material necessary for their growth, and partly to replace proteins lost in the ordinary wear and tear of tissue activity. Only part of the amino-acids in the circulation is apparently needed for those purposes, and there is no way of storing up a reserve of amino-acids as there is some of the other food substances. What is not required by the tissues is taken up by the liver and by enzymic action the amino part is separated from the rest—de-amination. The amino-free part is returned to the blood to be used up in energy production in the tissues, while the amino part is converted into urea and also returned to the blood stream in order to be excreted by the kidneys as a waste product.

In addition, to amino-acids from the digestion of foods, other amino-acids are continually being produced by the breaking down of protein matter in the body cells in the ordinary activity of these cells. These

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'endogenous' amino-acids are treated by the liver in the same way as the other 'exogenous' amino-acids.

Urea and certain other waste metabolic products, such as uric acid and creatinine, constitute the non-protein nitrogen content of the blood. A study of this gives considerable information about the functional capacity of the kidneys, which are mainly concerned in its excretion.

#### ESTIMATION OF BLOOD NON-PROTEIN NITROGEN AND UREA

The estimation of non-protein nitrogen in the blood is not quite easy in a small laboratory, because considerable laboratory experience and special apparatus are necessary. Standard methods are those of Folin and Wu, which require a colorimeter, and that of Kjeldahl.

It has been found, however, that the estimation of blood urea has for most purposes the same significance, especially as regards kidney function, as the estimation of the total non-protein nitrogen, of which it forms about half, and as easier methods are available for estimating blood urea, it is now generally used. Some of these methods also are not easy for the small laboratory including those of Folin and Wu and Van Slyke and Cullen.

A much easier method is that of Hensch and Aldrich (1926), and although it may not have the accuracy of the other methods the variations of the results from these are not of practical clinical significance. It is much better for the ordinary laboratory to use such a method than to attempt the more difficult time-consuming methods which in inexperienced hands may lead to considerable error.

#### HENSCH AND ALDRICH BLOOD UREA ESTIMATION

(1) Take 7 to 10 c.c. of blood in an oxalated tube. The best way of preparing an oxalated tube is to put into it 0.1 c.c. of a 30 per cent solution of chemically pure neutral potassium oxalate, rotate the tube to coat the walls and allow it to dry. If an examination is requested and a prepared tube is not available, about 20 mgm. and not more than 30 mgm. of powdered potassium oxalate is put into the tube for 10 c.c. of blood. If the blood has to be sent away for examination the following preservative anti-coagulant may be used in the bottle: 0.011 gram per c.c. of blood of a mixture of 1 part of thymol and 10 parts of ammonia-free sodium fluoride ground in a mortar and sieved through a 100 mesh sieve (Sander, 1923).

(2) Take equal volumes of oxalated blood and 10 per cent trichloroacetic acid, shake well, allow to stand for 5 minutes, and centrifuge. This precipitates the protein matter in the blood.

(3) Take 5 c.c. of the supernatant fluid and titrate it with 5 per cent mercuric chloride ( $\text{HgCl}_2$ ), using a burette. About 1.5 c.c. may be run in immediately; afterwards proceed slowly.

(4) To test the end point of titration take a porcelain tile or white plate and place on it several drops of a saturated solution of sodium carbonate. Dip the end of a glass rod into the blood extract being titrated and touch one of the drops of sodium carbonate. When the end point of titration is approaching, a yellow colour appears in the drop. A reddish brown precipitate appearing within 3 seconds shows the actual end point.

(5) The calculation of the blood urea is as follows: Multiply the number of c.c. of mercuric chloride used by 40 which gives the mercury combining power for 100 c.c. of blood; from the figure so obtained subtract 60 which represents the mercury combining power of substances other than urea; this gives the amount of blood urea in mgm. per 100 c.c. of blood.

#### SIGNIFICANCE OF BLOOD UREA FINDINGS

The normal blood urea in a fasting person is from about 10 to 40 mgm. per cent.

In referring to the figures given by different workers it will be found that some use the term 'urea nitrogen' and some 'urea'; these are not the same, but one gram of urea nitrogen corresponds to 2.14

grams of urea. Therefore if urea nitrogen figures are wanted, the figure obtained for urea should be divided by 2.14.

Variation in blood urea figures is brought about by:

- (1) The protein intake of food.
- (2) The volume of urine excreted.
- (3) Metabolic changes in the body including destruction of body protein.

(4) The abilities of the kidneys to excrete urea.

A diet abnormally high in proteins may raise the blood urea figures, especially if the amount of fluid taken is not abundant. Free diuresis lowers the figures, especially in conditions tending to nitrogen retention.

Destruction of body protein may raise the figures considerably, particularly if the urine output is small. Conditions producing destruction of body protein include: starvation, poisoning with various drugs, surgical shock, peritonitis, severe infection of all types, intestinal or pyloric obstruction, dehydration from any cause, intractable vomiting or diarrhoea as in cholera or dysentery, acute yellow atrophy of the liver, and the terminal stages of Addison's disease.

The estimation of blood urea is of no use in determining minor grades of kidney disability, but it is of considerable value in advanced grades. The removal of one kidney in an otherwise normal person makes no difference in blood urea readings; a marked rise is found only after about three-quarters of the kidney tissue has been destroyed, or put out of function. High figures are found most often at the height of an acute attack of glomerular nephritis and in the advanced stages of chronic glomerular nephritis. In the terminal stages very high figures may be found, from 150 to 300 mgm. or even more.

The estimation of blood urea is useful in differentiating between renal and cardiac disorders, as there is no increase in the latter.

In the treatment of renal disorders repeated blood urea estimations are a valuable method of prognosis and guidance in treatment.

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 STITT, E. R., CLOUGH, P. W., and CLOUGH, M. C. *Practical Bacteriology, Haematology and Animal Parasitology*. 9th Ed.  
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### The Effect of Different Environmental Temperatures on the Survival of Dogs after Severe Bleeding

By R. A. CLEGHORN, M.D., D.Sc. (Aberd.)

(Abstracted from the *Canadian Medical Association Journal*, Vol. IXL, November 1943, p. 363)

#### SUMMARY

1. The influence of different environmental temperatures on the survival of critically-bleed dogs has been investigated.

2. The mortality at four different temperatures was as follows: 18 per cent at 72°F.; 38 per cent at 52°F.; 45 per cent at 85°F.; and 93 per cent at 95°F.

3. The higher mortality in the dogs at 52°F. compared with those at 72°F. is ascribed to the increased oxygen requirement.

4. The higher mortality in the dogs at 85°F. compared to those at 72°F. is attributed to the deleterious influence of vasodilatation caused by this degree of warming. The insensible water loss in this group was not a factor as it was the same at both temperatures.

5. The higher mortality in the dogs at 95°F. compared with those of 72°F. is ascribed to vasodilatation and to increase in insensible water loss associated with the panting which occurred at this temperature.

6. In another group of dogs exposed to 95°F. an amount of water equivalent to the increase in the insensible water loss was given. The mortality in this group was reduced to approximately that seen in the dogs exposed to 85°F.

7. The differences in the responses of dogs and man to elevation of the environmental temperature are briefly discussed and the reasons why patients who are suffering from secondary shock or severe acute hæmorrhage should not be heated are cited.

### Autopsy Nerve Grafts in Peripheral Nerve Surgery

By R. M. KLEMME

R. D. WOOLSEY

and

N. T. DEREZENDE

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIII, 16th October, 1943, p. 393)

THE first clinical application of eadaver graft, using 50 per cent acacia to glue the severed ends together, has been made. The first patient already has a good clinical result with return of motor and sensory function. The second patient is already beginning to get return of function. The third case is too recent to make it possible to judge.

The post-operative care of a patient operated on with a peripheral nerve injury is a very important factor for recovery. Any method that can increase the local circulation will be of primary importance in the process of physiologic recovery.

### Heavy Density of *Plasmodium falciparum* Parasites in Malaria

By A. N. SPRINGALL

(Abstracted from the *American Journal of Tropical Medicine*, Vol. XXIII, September 1943, p. 533)

THE schizont and merozoite forms of *P. falciparum* are not seen in the peripheral blood except in rare instances in very severe infections, which are moribund cases. Ross estimated that in a severe infection the parasites may number 12 per cent of the erythrocytes. Hackett states that the parasites can soar to fantastic heights in fatal cases just before death, in which parasites occupy every third red cell. Bignami and Marchiafava mention a case in which about half of the red blood cells was parasitized.

The fatal case reported showed all forms of the asexual cycle of development of *P. falciparum* in the peripheral blood. Forty-four and two-tenths per cent of the erythrocytes were infected; approximately one-third of the infected cells contained multiple parasites; there were 66.8 parasites for every 100 erythrocytes.

If the suppositions are accepted that this patient had a total blood volume of five litres, and that he had 2,000,000 red blood cells are cubic millimetre of blood, it may be estimated that there were 6.68 trillion parasites in his body.

This case exhibited the heaviest infection of *P. falciparum* that has been studied at Gorgas Hospital in recent years; and no hospital record can be found of a heavier infection in previous years.

### The Absorption Rate from the Bone Marrow

(From the *Medical Press and Circular*, Vol. CCXI, 12th January, 1944, p. 18)

SINCE 1940, the medullary cavities of the sternum and long bones have been used for the introduction of blood plasma and other fluids. Several observers have reported favourably on the value of this procedure in patients with extensive burns of the extremities, in patients with extreme shock and peripheral vascular collapse, and in dehydrated infants. The procedure is easy and the injected fluids are rapidly absorbed. This is shown by the clinical improvement of the patients and by experiments in man and animals.

The authors report an experiment in which an effort was made to determine in actual time, the absorption rate from the marrow as compared with the absorption rate from the vein. Circulation times were done by injecting 3 c.c. of a saturated solution of saccharin into the median basilic vein of twenty-four patients. The next step was the injection of an equal amount of the same solution into the sternal marrow of the same patients soon after the intravenous test. The site of injection was in the middle of the body of the sternum at the level of the third interspace. A survey of the results indicates a distinct consistency in the circulation times for the individual subjects; it was essentially the same in twenty-one subjects. In two cases of cardiac decompensation the circulation time from the marrow was less than by the venous route; in a third case the results were identical.

The authors conclude that these results are further proof of the intimate relationship between the medullary cavities and the general circulation and warrant the use of intramedullary injection of fluids when venous channels are not readily accessible.

## Reviews

**ACUTE INJURIES OF THE HEAD: THEIR DIAGNOSIS, TREATMENT, COMPLICATIONS AND SEQUELS.**—By G. F. Rowbotham, B.Sc. (Manch.), F.R.C.S. (Eng.). 1942. E. and S. Livingstone, Edinburgh. Pp. xii plus 288, with 124 illustrations, 12 in full colour. Price, 25s.

THIS is a model of what a monograph should be, and a credit to both the author and to the publishing house, whose name is fast becoming a guarantee of a craftsmanship unexcelled in medical book production.

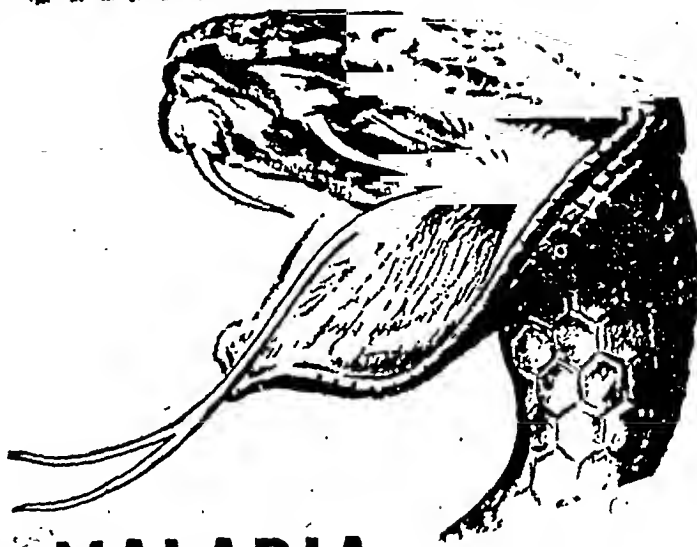
The text is a short but comprehensive account of all the problems likely to confront the general surgeon faced with the management of acute head injuries. It is written in a simple style which is easy to follow and is amply supported by a wealth of appropriately selected and well-reproduced illustrations.

The first part of the monograph deals lucidly with the mechanisms and the pathology of cranio-cerebral

injury. Closed head injuries are then dealt with succinctly, and the remaining part of the book deals with open wounds—so profoundly significant in these times and with their sequelae and complications.

While all of the book is excellent, the chapters dealing with operative treatment are particularly praiseworthy, and constitute a reliable guide to surgeons called upon to care for such cases without a background of special neuro-surgical experience. The procedures are very practical, and are both adequately described, and well illustrated. If followed, the author's advice will go far to negative the lack of specialized training. There are too few trained neuro-surgeons to cope with all the present-day problems of cranio-cerebral injury; too frequently, it is economically essential to establish the neuro-surgical centres at large, central areas, or at the surgical base. So that a good deal of the immediate—and often the all-important—primary care becomes the

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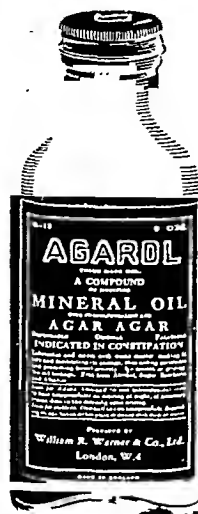


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province of the general surgical practitioner. We believe that if all of these general surgeons were to follow this practice outlined in this wise and judicial manual, some at least of the tragic disasters which the neuro-surgeon sometimes lays at the general surgeon's door would be avoided.

I. B.

**A SYNOPSIS OF SURGICAL ANATOMY.**—By Alexander Lee McGregor, M.Ch. (Edin.), F.R.C.S. (Eng.). Fifth Edition. 1943. John Wright and Sons Limited, Bristol. Pp. xiii plus 710, with 696 illustrations. Price, 25s.

THE fifth edition of this book now appears. The main alterations are that the chapters on the anatomy and surgery of the sympathetic have been re-written and new sections appear dealing with the supraspinatus tendon, the subdeltoid bursa, and the intervertebral disc. The paper, necessitated by war conditions, is rather poor. The heavy type used in many places tends to show through. The tabular form in which the book is written does not make for easy reading; it does make it easy to make it a book of reference on particular points which can be easily traced. There are 696 figures, all line drawings some of which are very diagrammatic. More natural illustrations would have been welcome in many places.

J. L.

**ILLUSTRATIONS OF REGIONAL ANATOMY.**—By E. B. Jamieson, M.D. Section I:—'Central Nervous System' containing 50 plates. Section II:—'Head and Neck' containing 64 plates. Section III:—'Abdomen' containing 44 plates. Section IV:—'Pelvis' containing 35 plates. Section V:—'Thorax' containing 32 plates. Section VI:—'Upper Limb' containing 42 plates. Section VII:—'Lower Limb' containing 52 plates. Fifth Edition. 1944. E. and S. Livingstone, Edinburgh. Price, 75s. and postage, 10d.

THESE illustrations now in their fifth edition are in seven sections: central nervous system, head and neck, abdomen, pelvis, thorax, upper limb, and lower limb. Each section is obtainable separately, and cloth-bound copies of the complete set are also obtainable. Each section consists of a list of plates and the plates themselves, varying in number from 32 to 64, the total number of plates being 390. The plates consist of diagrams very clearly printed on thick and heavy art paper, and all the features of the diagrams are very clearly labelled. The diagrams are in colour, in some cases nine colours being used. Each plate is easily removable because of the loose leaf folder, which is very strongly made.

This set of illustrations of regional anatomy is a magnificent production. We have never seen before such a fine set. They should be of great use to medical students and also to budding or even experienced surgeons. A physician can also learn much from them. The price of the set is high, 75s., but this price is justified by the fine quality and large number of the illustrations all on heavy art paper.

J. L.

**DISEASES OF THE HEART. DESCRIBED FOR PRACTITIONERS AND STUDENTS.** By Sir Thomas Lewis, C.B.E., F.R.S., M.D., D.Sc., LL.D., F.R.C.P. Third Edition. 1943. Macmillan and Company, Limited, London. Pp. xx plus 297. Illustrated. Price, 15s.

THIS book was first published in 1933 and since then has been a standard book on the subject. The second edition appeared in 1937, the third in 1942. This is a reprint of the third edition. It is unnecessary here to discuss the many merits of this book which has won many admirers. All the publications of Sir Thomas Lewis are distinguished by good matter based on wide personal experience and sound presentation in good and simple English. His writings present 'a natural and logical sequence of ideas and not simply a series of

disconnected facts'. This is what makes them so very readable. They stimulate the reader to the careful and systematic observation of his cases and to the attempt at sound and logical deductions from those observations.

J. L.

**CHEST EXAMINATION: THE CORRELATION OF PHYSICAL AND X-RAY FINDINGS IN DISEASES OF THE LUNG.**—By Richard R. Trall, M.C., M.A., M.D. (Aberd.), F.R.C.P. (Lond.). 1943. J. and A. Churchill Limited, London. Pp. x plus 107. Illustrated. Price, 10s. 6d.

ALTHOUGH radiology has, to a large extent, switched the attention of students and practitioners off the physical examination of chest to the x-ray finding for the final opinion, the former should always have the first place, while the latter is to be reserved for confirmation of the clinical observations and not used as a substitute. It is only by careful correlation of the physical and radiological findings that a true diagnosis can be made. We therefore welcome Wing Commander Trall's book, and hope that it will stimulate a revival of the study and importance of physical signs of chest diseases.

This little book consists of four parts. The first section deals with applied anatomy including the normal x-ray appearance of the chest. The second is on applied pathology and gives a brief account of the abnormal findings in common pulmonary diseases and the correlation of the morbid changes, physical signs and x-ray findings, the aim being to give an idea of what is happening inside the chest. The next section is devoted to physical examination and details of only such aids and points which the author has found of special interest to post-graduates. This is followed by a short reference to the interpretation of abnormal chest films. Some of author's statements are open to criticism and the discussion of some points is too brief to be of much value.

R. N. C.

**CABOT AND ADAMS' PHYSICAL DIAGNOSIS.**—By F. Dennette Adams, M.D. Thirteenth Edition. 1942. Baillière, Tindall and Cox, London. Pp. xv plus 888, with 398 illustrations. Price, 27s. 6d.

THIS book, originally published in 1900, went through eleven editions in 34 years without very drastic revisions. In 1937 a complete revision was undertaken by Dr. Adams, and this formed the twelfth edition. The present edition is the thirteenth, and the changes in this edition are described in the preface as follows:

'In this one it has been necessary only to recognize where greater clarity could be achieved and to emend where competent reviewers and my own reflection suggested it. I have added such new material as, in the light of recent experience, has seemed valuable. The sections on the mouth, back, pulse, classification of heart murmurs, and coronary heart disease have been thoroughly reorganized. The chapter on congestive failure has been supplemented by the addition of a section on inadequate cardiac output. Elsewhere I have added to the list of clinical entities discussed.'

'In the first eleven editions, Dr. Cabot followed the plan of describing only those techniques which he himself thought valuable and discussing only those aspects of disease with which he had personal experience. The twelfth and present editions are based not on what Dr. Cabot called "the personal equation" but on quite the opposite principle; to-day no one person's experience is sufficient to include all that the student of physical diagnosis should know. As in the twelfth edition, I have again drawn freely on the experience of colleagues at the Massachusetts General Hospital and of friends in other hospitals whose specialized knowledge in their own fields gives their opinions particular value. Like its predecessor, this edition may be said to represent as far as possible a cross section of the views on diagnosis held by the staff of the Massachusetts General Hospital.'

'The general purpose of the book remains the same: to show how we think the patient should be examined



to describe and interpret important symptoms and signs, and briefly to discuss the more common disorders in which they occur?

'The occasional criticism has been voiced so that a text on physical diagnosis should not contain discussions of clinical entities. I can only emphasize again my conviction, on which the twelfth edition was based, that physical signs can be intelligently taught and intelligently learned only in their relationship to and not apart from the other aspects of disease.'

The reviewer happens for many years to have been engaged in a special branch of medicine but has recently returned to more general medicine. During the last year he has read a large number of books on general medicine but he can truthfully say that there is no book he has read which he has found so valuable as this one. Physical diagnosis in these days of laboratory medicine tends to be neglected. A periodical reading of this book can be recommended to those in general practice and in specialized practice as possibly the best method of improving one's standard of medical practice. Excellently printed on good paper, well bound and with nearly 400 illustrations, it is splendid value for money.

J. L.

#### STEDMAN'S PRACTICAL MEDICAL DICTIONARY.—

By Stanley Thomas Garber, B.S., M.D. Fifteenth Revised Edition. 1942. Baillière, Tindall and Cox, London. Pp. xv plus 1257. Illustrated. Price, 42s.

This is a fifteenth edition of the dictionary and possibly the best of its kind. It has been thoroughly revised and completely reset in new type. Hundreds of new titles have been headed and numerous obsolete terms have been omitted.

A fine production.

J. L.

#### BOOKS RECEIVED

1. A Descriptive Atlas of Radiographs: An Aid to Modern Clinical Methods. By A. P. Bertwistle, M.B., Ch.B., F.R.C.S. (Edin.). Fifth Edition, Revised and Enlarged. 1942. Published by Henry Kimpton, London. Pp. xxxii plus 584, with 879 illustrations. Price, 42s.

2. The British Encyclopædia of Medical Practice including Medicine, Surgery, Obstetrics, Gynæcology and other Special Subjects: *Surveys and Abstracts, 1941-42 and Cumulative Supplement, 1941-42.* Under the general Editorship of Sir Humphry Rolleston, Bt., O.C.V.O., K.C.B., M.D., D.Sc., D.C.L., LL.D. Butterworth and Company, Limited, London. Pp. vi plus 432 plus 49 in Surveys and Abstracts and Pp. 289 in Cumulative Supplement. Price (not stated).

3. Alarming Heart Attacks—Serious and Innocent. By H. O. Gunewardene, M.B., B.S. (Lond.), D.M.R.E. (Cantab.). Published by the author. Printed at the Ceylon Daily News Press, Lake House, McCallum Road, Colombo. Pp. 61. Illustrated. Price (not stated).

4. Gold Therapy in Tuberculosis. By Dr. C. Dwarakanath, L.I.M. (Madras) and Z.T. (Hamburg 'Varsity'). 1943. Published by the author, 'Nut Shell', Kilpauk, Madras, and Printed by Gordon and Company, Limited, Triplicane, Madras. Pp. ii plus 61. Illustrated. Price, Rs. 2-8.

5. Climate and Labour: An Enquiry into the Influence of Climate on Mental and Physical Work. By W. Burridge, D.M., M.A. (Oxon.), F.N.I., F.N.A.S. 1944. (Lucknow University Studies.) Messrs. Kitabistan, 17A, Kamala Nehru Road, Allahabad. Pp. 167. Price, Rs. 5-4.

6. Psychopathology: A Survey of Modern Approaches. By J. Ernest Nicole, L.M.S.S.A., D.P., M.R.C.P. & S. Third Edition. 1942. Baillière, Tindall and Cox, London. Pp. xi plus 265. Price, 16s.

7. Hermaphrodites. The Human Intersex. By A. P. Cavadias, O.B.E., M.D., F.R.C.P. 1943. William Heineman Medical Books Limited, London. Pp. ix plus 78. Illustrated. Price, 15s.

## Correspondence

### NOVARSENOBILLON AND MAPHARSIDE IN THE TREATMENT OF THE ATTACK OF MALARIA

SIR,—I was greatly interested in your paper on the treatment of the attack of malaria by novarsenobillon and mapharside published in the March 1944 issue of your *Gazette*. In the last paragraph of your paper you mention the possibility that combined treatment of one of the organic arsenicals with quinine might possibly reduce the relapse rate considerably. This question I have tried to answer in a number of cases too small yet for publication but with such encouraging results that this short note appears already justified.

From time to time I am consulted by patients giving a long history of frequent relapses of malaria in spite of sufficient treatment with quinine as well as atabrin. Blood examination during the relapse reveals the presence of *Plasmodium vivax*. For the same reasons as stated by you that one can never be quite sure that there may not be also an infection with *P. falciparum* I have not felt justified in starting treatment at once with neoarsphenamine or mapharside but have always begun treatment with two or three days quinine followed by four or five intravenous injections of neoarsphenamine or mapharside. In all of these cases with the exception of one the result has been cessation of attacks. This treatment was also given to one patient who suffered from a chronic infection of *P. falciparum* with numerous attacks of low fever and also some attacks of very high temperature. After a holiday in the hills of four weeks he was suffering from an attack in Calcutta while on his way to Assam. The combined quinine mapharside treatment kept him free from attacks for over six months when he fell ill again, but this time with tertian malaria, obviously a new infection.

The number of my cases of this relapsing type treated in the way described above is statistically insignificant. They comprise only about ten cases, and one relapsed after the treatment. All the others lost their malaria infection by this method after a history of many months of unsuccessful treatment with sufficient amounts of quinine and atabrin.

RUDOLF TREU, M.D., L.R.C.P., etc.

43, CHOWRINGHEE ROAD,

CALCUTTA,

11th April, 1944.

[Note.—It is believed that studies are now being made in India on the value of the neoarsphenamines in combination with quinine and atabrin in the prevention of malaria relapses, and that the results have not been very encouraging.]

General experience indicates that the value of arsenic in *P. falciparum* infections is very little.—EDITOR, I. M. G.]

### NAGA SORE

SIR,—Recently I read with interest the 'Report on the Occurrence of Naga Sore in Calcutta' by Drs. Panja and Ghosh in your January issue.

In my sixteen years' practice, the disease was rarely found here, though it has been always endemic in the hilly parts 30 to 40 miles off from this tea estate. In 1942, some labourers who were sent for road work to the hills near the Burma border returned with typical Naga sores in their lower extremities, and since then the disease has been endemic here. The doctors of the neighbouring tea estates have also similar experience. So, I quite concur with the view of the authors that the original source of the infection was from imported cases amongst the evacuees from Burma passing through Assam.



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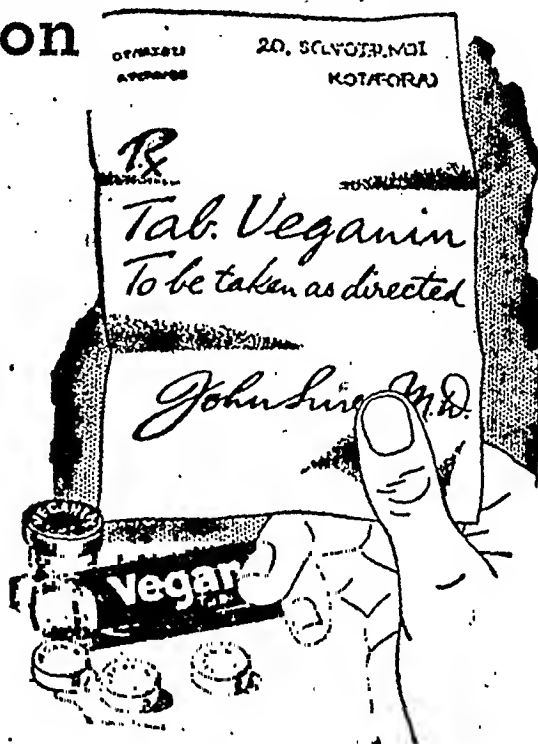
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Lastly with regard to the line of treatment suggested by the authors, may I say that cauterization of the sore with pure nitric acid is very effective in clearing the slough within 3 or 4 days?

The technique is:—

- (a) Clean the ulcer as much as possible off the superficial slough.
- (b) Cauterize it with a swab dipped in pure nitric acid (preceded by an injection of morphia in case of extensive or multiple sores) and immediately wash the part with normal saline or pure water.
- (c) Put a simple dressing for the day.
- (d) From the second day onwards, dress the ulcer with sulphanilamide powder once daily until it is filled up with healthy granulation tissue when a simple antiseptic ointment may be applied.

I have found the above treatment very successful in my cases in completing a cure in 2 to 3 weeks' time.

B. L. SEN, L.M.F.,  
Assistant Medical Officer,  
Samdang Tea Estate.

DOOM DOOMA P. O.,  
ASSAM,  
21st April, 1944.

### STERNAL PUNCTURE

SIR,—In recent books on hæmatological technique there is often no reference to the possibility of sepsis of the manubrium sterni, following sternal puncture.

When sternal puncture first came into common use for hæmatological and kala-azar investigations, two cases in my wards at the Mayo Hospital, Lahore, developed septic infections of the bone marrow and osteomyelitis of the manubrium, leading to long and serious illnesses.

The practice was then begun of preparing the skin 24 hours before the puncture, as for a surgical operation, and of nicking the skin with a sharp knife, so that the sternal puncture needle does not pass through the actual skin.

Hearing of two recent cases of osteomyelitis of the manubrium, one of which led to septicæmia, has prompted me to write this note.

Experience shows that the greatest aseptic care is essential for any type of paracentesis or puncture of an internal organ. It is recommended that the technique suggested above be used in all cases where a needle is inserted into an internal organ, i.e. pleura, liver, spleen or peritoneum, in such cases as pleural effusion and empyema, liver abscess, and ascites.

Such procedures are too often left to the recently qualified house man or the inexperienced medical officer, without precise instructions of the essential technique.

G. F. TAYLOR,  
COLONEL, I.M.S.

C/O DIRECTOR OF MEDICAL SERVICES  
IN INDIA, GENERAL HEADQUARTERS,  
INDIA, MEDICAL DIRECTORATE,  
NEW DELHI,  
2nd April, 1944.

## Service Notes

### APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL J. C. PYPER, O.B.E., I.M.S. (Retired), assumed charge of the Office of the Civil Surgeon, Lahore, on the afternoon of the 31st March, 1944, relieving Major C. F. Garfit, Deputy Inspector-General of Civil Hospitals, Punjab, of the additional charge from the same hour and date.

Lieutenant-Colonel J. H. Gorman has been appointed as Director of Inspection in the Department of Food

(Division III), with effect from the 12th April, 1944 (forenoon).

Lieutenant-Colonel D. Kelly has been appointed as Medical Officer, Pachmarhi, with effect from 20th April, 1944.

The services of Major C. J. Hassett, M.B.E., an Agency Surgeon, are placed at the disposal of the Government of India in the Department of Education, Health and Lands, with effect from the afternoon of the 15th March, 1944.

Major H. A. Ledgard is appointed as Civil Surgeon, Quetta/Sibi, with effect from the forenoon of the 17th March, 1944.

Major C. J. Hassett, M.B.E., Agency Surgeon, North Waziristan, Agency Surgeon, Tochi, and Medical Officer, North Waziristan Scouts, Miran Shah, is appointed Civil Surgeon, Ajmer, with effect from the 25th March, 1944.

Major G. B. W. Fisher made over medical charge of the Daeca Jail Hospital to Colonel H. J. Curran, on the 2nd April, 1944.

Major J. H. Caverhill on general duty attached to Surgeon-General's Office, is temporarily appointed as Civil Surgeon, 24-Parganas, vice Lieutenant-Colonel K. S. Thakur.

(Permanent Commission)

To be Captain (on probation)

Nowshir Jungalwalla. Dated 1st February, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

Dinanath Chatterjee. Dated 20th December, 1943.

Mohammed Sharif Khan. Dated 15th January, 1944.

Kumud Chandra Dhar. Dated 20th January, 1944.

Clement Somasundaram David. Dated 26th January, 1944.

Himanshu Mohan Kar. Dated 6th February, 1944.

Sohrab Hormasji Kutar. Dated 7th February, 1944.

Pillalamarri Ramakrishnamurthy. Dated 15th February, 1944.

Kolipaka Gopalakrishna Rao. Dated 18th February, 1944.

Lokendra Nath Banerjee. Dated 20th February, 1944.

Kashi Ram Mahajan. Dated 22nd February, 1944.

INDIAN MEDICAL SERVICE—FOR SERVICE WITH THE ROYAL  
INDIAN NAVY

(Emergency Commission)

To be Captain

Narendra Sammukhlal Shroff. Dated 24th January, 1944.

The undermentioned officer of the I.M.S. (E.C.) reverts from the Royal Indian Navy and is seconded to the I.A.M.C.:—

LAND FORCES

(SECONDED TO INDIAN ARMY MEDICAL CORPS)

(Emergency Commission)

Lieutenant R. T. Hinde. Dated 25th February, 1944.

To be Lieutenants

14th January, 1944

Ramasubramanian Muthu Krishnaswamy.  
Ramachandra Purshotaman.

15th January, 1944

M. Dakshina Murthy. Manel Krishna Nayak.  
Zahiruddin Ahmad. Shamsul Abedin.  
Abdul Rahman Khan.

18th January, 1944

Kazimannil Jacob Verghese.  
Puthalpet Guruswamy Kesavalu.  
Mayer Ezeikel Roby.  
Krishnaswamy Srinivasa Raghavan.

19th January, 1944

Rasamay Ganguly.  
S. Mohana Krishnan.  
Ramchandran Narayanan.  
Shimoga Ranganannayara Ganeshiya.

20th January, 1944

Kruttiventi Ganga Visveswara Bhagavannarayana.  
C. Thomas Simon.  
Karisulndamangalam Sundaramiyer Ramakrishnan.  
Jesudoss Jothinayagam Barnes.  
Mandayam Anandampillai Ramaswamy.  
T. A. Abdul Gafur.  
Tiruppattur Subramanya Kalyanam.  
Valangiman Ramamoorthy Srinivasan.  
Cheriachanasseri Raman Aiyappan.  
Karra Umamaheswara Rao.  
Mathai Thomas. Dated 21st January, 1944.  
Koka Mohan Rao. Dated 20th February, 1944.  
Jibon Krishna Adak. Dated 21st February, 1944.

## INDIAN LAND FORCES

SECONDED TO INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

(WOMEN'S BRANCH)

*To be Captain*

(Mrs.) Saguna Bai Mangalore. Dated 1st January, 1944.

*To be Lieutenants*

(Miss) Kamala Nihal Chand Lai. Dated 15th January, 1944.  
(Miss) Daisy Elizabeth Thomas. Dated 24th January, 1944.  
(Miss) Shyam Mohini Terway. Dated 14th February, 1944.  
(Miss) Lila Balkrishna Bhawe. Dated 15th February, 1944.

## PROMOTIONS

*Major to be Lieutenant-Colonel*

J. Quigley. Dated 1st March, 1944.

*Captain to be Major*

S. Rameshwar. Dated 5th March, 1944.

## INDIAN LAND FORCES

SECONDED TO INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

*Lieutenants to be Captains*

A. W. Sunderanathan. Dated 16th November, 1943.  
Z. A. Siddiqui. Dated 13th February, 1944.  
R. C. Sharma. Dated 22nd February, 1944.

1st March, 1944

A. J. Cadogan. P. W. Weston.  
St. J. L. Wling. S. C. Gomez.

2nd March, 1944

N. G. I. Govindaraj. S. F. Gomez.  
H. R. E. Gillespie. C. H. Cousins.

5th March, 1944

E. A. Tarleton. P. R. Pires.  
D. D. Stidston. D. P. D'Vaz.  
C. R. Peck. D. D. G. Passanha.

6th March, 1944

S. O. Waller. H. B. Gibson.

7th March, 1944

D. J. R. Snow. D. W. Shillong.

12th March, 1944

G. L. Banerjee. D. J. Toomey.  
J. Bakht. Dated 18th March, 1944.  
K. K. Bose. Dated 22nd March, 1944.  
S. K. R. Chaudhuri. Dated 24th March, 1944.  
A. P. Muruff. Dated 27th March, 1944.  
K. M. Bose. Dated 28th March, 1944.  
C. W. R. D'Rozario. Dated 5th February, 1943.

S. K. N. Sinha. Dated 17th June, 1943.  
J. M. Thornton. Dated 8th August, 1943.  
P. L. F. Heaton. Dated 18th August, 1943.  
G. M. F. Dover. Dated 28th August, 1943.  
S. H. Montgomery. Dated 12th September, 1943.

## INDIAN LAND FORCES

(SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY)

(Emergency Commissions)

*Lieutenants to be Captains*

12th March, 1944

B: N. A. Beetles. P: A. R. V. Ross.  
V. C. D. Sausman.

C. A. Hanson. Dated 16th March, 1944.

(WOMEN'S BRANCH)

*Lieutenants to be Captains*

(Miss) H. Malik. Dated 26th February, 1944.  
(Miss) T. N. Irani. Dated 23rd March, 1944.

## RETIREMENT

Lieutenant P. A. C. Davenport. Dated 1st April, 1944.

## RELINQUISHMENT

The undermentioned officer relinquishes the local rank of Major on ceasing to be employed as a Senior Recruiting Medical Officer:—

Captain S. D. Butt, I.M.S. (E.C.). Dated 1st January, 1944.

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## Original Articles

# TETANUS NEONATORUM IN THE TROPICS A SUGGESTION FOR ITS REDUCTION

By SIR LEONARD ROGERS, K.C.S.I., M.D., F.R.C.P.,  
F.R.S., I.M.S. (Retd.)  
London

ABOUT forty years ago I found that placing a very small amount of the dust of Calcutta streets under the skin of rats caused five out of six of them to die of tetanus. That disease was then very common among the surgical admissions into the Medical College Hospitals with wounds contaminated with street dust, but my advocacy of the administration of prophylactic doses of antitetanic serum on admission of such cases led to a great decrease in the post mortems on tetanus cases. In an analysis of 1,600 post mortems performed by me in Calcutta, recorded in my Findlayson lectures of 1925, I showed that 2.05 per cent of the total deaths were due to tetanus; compared with only 0.1 per cent, twenty times less, in 1,000 post mortems at a London hospital. I also quoted Calcutta's vital statistics to show that 6.04 per cent of the total deaths were due to tetanus, with 906 such deaths in 1921, 785 of which were in children up to five years of age. The great majority of these are well known to be cases of tetanus neonatorum due to Indian *daïs* or midwives dressing the severed umbilical cords of new-born infants with cow-dung and other filthy applications.

In China, tetanus neonatorum has been reported to be appallingly frequent, and a similar high incidence is likely to occur in other tropical countries with backward sanitary customs, such as New Guinea where tetanus is also reported to be common. The treatment of tetanus neonatorum cannot be expected to be successful in many of the cases, although recoveries are on record. It is therefore worth while considering if anything can be done to lessen the present terribly high incidence of the disease among infants born in tropical countries, apart from the very slow progress of improved social customs.

*Immunization against tetanus.*—Active immunization against tetanus by injections of the toxoids of Ramon has been compulsory in the French army since 1936. In 1938 Boyd extended their use on a voluntary basis to the British army, and in 1940 Perry reported that there had been no case of tetanus among the 80 to 90 per cent of about 850,000 men of the British Expeditionary Force in France who had accepted inoculation against the disease, in spite of the circumstances of the fighting making it impossible to administer antitoxic serum in the majority of the wounded; cases of tetanus were only reported among the 10 to 20 per cent who

had rejected immunization against the disease. Moreover, in the Middle East troops, Boyd and MacLennan in 1942 reported a tetanus incidence of only 0.13 per 1,000 wounded among the immunized, compared with 1.6 per 1,000 among the unimmunized, or 12.8 times fewer than among the unimmunized. Of the five cases that occurred among the immunized, 2 recovered; of the three fatal cases 2 showed extensive necrosis and sepsis of the tissues of their wounds, so that had the essential adjunct to immunization, the removal of the damaged tissues, been available, these patients might very probably also have been saved. There is thus very strong evidence now available regarding the protective value of active immunization against tetanus in the case of infected war wounds.

*Methods of tetanus immunization.*—In recent years much research work has been carried out by British army investigators and others to determine the immunological response in relation to the number and spacing of the doses of tetanus toxoid. It is generally recognized that the first dose produces little or no antitoxin in the blood, but it appears to sensitize the reticulo-endothelial system over a period of about six weeks, at the end of which time a second dose of 1 c.cm. of toxoid results in an out-pouring of tetanus antitoxin into the blood to reach 0.1 to 1 unit per c.cm. after the lapse of a further 10 to 12 days, after which it declines very slowly. A third dose given six months later causes a remarkable rise of the antitoxin titre to reach, as a rule, 2 to 10 units per c.cm. of the patient's serum, an effective level in the case of wounded soldiers who receive early and adequate surgical treatment. In the American army an additional 'boosting' dose is given shortly before the men proceed on active service; in the British army it is now the rule that an additional dose of toxoid is administered to all the wounded still further to increase their resisting power against the very dangerous tetanus infection. In 1941 Evans reported that the antitoxin level in the blood is substantially maintained for ten months after the second injection; and that a third dose after that interval results in a rapid and large increase in the antitoxin level of the serum, which is maintained substantially unchanged for a month. Marvell and Parish (1940) also reported that a third injection given at an interval of seven to nine months after the second had a greater immunizing effect than when given at an earlier date; this increase more than counteracted the waning effect of the immunity during the interval.

There is very general agreement that adults do not show in their serum any material amount of naturally acquired tetanus antitoxin, as so commonly occurs in the case of diphtheria as the result of sub-infective doses of diphtheria bacilli gradually acquired through contact with carriers of the latter organism. Thus, Evans (1941) did not find as much as 0.01 international unit of tetanus antitoxin per c.cm. of the serum



of any of the 81 persons aged 15 to 60 years. Even in the case of those specially exposed to possible contact with the tetanus bacillus, Lahiri (1939) found no tetanus antitoxin. There is therefore no likelihood of new-born infants having even a slight degree of immunity to tetanus, such as is commonly met with in the case of diphtheria in infants during the first year of their lives.

*Can infants be protected against tetanus neonatorum by immunizing their mothers during their pregnancies?*—In this connection it is of interest to note that Marvell and Parish in 1940 observed that women responded much better than men to tetanus toxoid injections. There seems good reason to expect that tetanus antitoxins developed in the blood of pregnant women by means of toxoid injections will be transmitted to the child she is carrying, as occurs in the case of diphtheria antitoxins, although I have not found any records of this having been experimentally tested.

The object of this note is to suggest that this possibility should be investigated at the Calcutta School of Tropical Medicine with the help as regards clinical material of the Eden and Dufferin Hospitals by determining the tetanus antitoxin titre of the serum of the immunized mothers and of their newly-born infants. If this test should demonstrate that practically important amounts of tetanus antitoxin are transmitted to the infants, it will clearly be advisable to immunize as many mothers as possible during the prenatal period by means of two doses as early in the pregnancy as proves to be practicable, and to give an additional dose ten days before the expected date of delivery to provide the maximum protection of the babes against the frequent and deadly tetanus neonatorum of tropical countries.

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### POLYNEURITIS

#### WITH SPECIAL REFERENCE TO THE ACUTE VARIETIES

By M. A. PIRZADA, M.B. (Pb.), M.R.C.P. (I.),  
D.P.H., D.T.M. & H. (Cambridge)

*Clinical Assistant to the Professor of Clinical Medicine,  
King Edward Medical College, Lahore (Late Lecturer  
in Clinical Medicine, Medical School, Amritsar)*

#### Introduction

CHRONIC polyneuritis is a clinical entity with which most practitioners are familiar. The diagnosis is easy and an ætiological factor can often, not always, be discovered. What perhaps may not be so familiar is polyneuritis of acute onset occurring in persons apparently

completely healthy with no obvious dietetic deficiency or toxic or infective factor. The diagnosis presents difficulties, and the ætiological factor is usually untraceable. That acute polyneuritis is not an unusual occurrence is indicated by the fact that the writer observed six cases in a period of nearly two years at the V. J. Hospital, Amritsar. An account of these cases follows. A brief reference has been made to five cases of chronic polyneuritis which were observed in the same period to give an idea of the relative frequency of the two types of polyneuritis in the experience of the writer.

#### Case reports

Group I: Polyneuritis with acute onset and negative Wassermann reaction.

*Case 1.*—A well-nourished healthy looking student, aged 20, was admitted on 1st May, 1943. Soon after excessive physical exertion on 2 successive days involving the carrying of heavy weights in hot weather he began to feel pain in the back and upper limbs and some stiffness of the neck. This sensation lasted 3 to 4 days. One of the legs then felt weak and he began to have some difficulty in micturition and defæcation. The symptoms gradually increased for another 3 to 4 days and the other leg became involved. On admission he was unable to walk, to sit up in bed without the use of arms, to pass urine or to defæcate. He complained of a sense of oppression in the chest and some stiffness in his neck. The lower extremities showed loss of deep reflexes, Babinski sign absent on both sides. Abdominal reflexes absent. The superficial sensations were dull below the knee but not lost, there was no muscular tenderness. No pains. The upper extremities were practically normal. No fever. Physical examination of the rest of the nervous system and other systems negative. No infective foci. Urine negative. Blood W.R. negative, C.S.F. negative. There was no recent history of exanthemata. A previous history of typhoid fever 7 years ago. No history of drug taking. Dietetic history did not reveal anything out of the ordinary. The patient was placed on massive doses of vitamin B<sub>1</sub> by injection. The condition improved steadily. Bladder and intestines started functioning on the 5th day of treatment and were in full function on 10th day. Power in legs started improving on the 5th day and by the 10th patient was able to sit up in bed without support.

On 25th May, 1943, when the patient was discharged he was capable of walking without support but right leg still showed weakness. Sensation of legs normal.

On 4th June, 1943, patient presented himself again. He said he was quite all right but that the right leg was still somewhat heavy.

*Case 2.*—A college lecturer was admitted on 21st May, 1942, with a history of sudden weakness developing in the legs and spreading to the arms 3 to 4 days previously. On admission the patient was helpless, had flaccid paralysis of all four extremities with wrist-drop and foot-drop and some weakness of the trunk. There were marked sensory symptoms with tingling and pains in the limbs, especially the legs, and marked muscular tenderness. Pains were severe at night. Stocking anaesthesia present in the legs, but no demonstrable sensory loss in the arms. Babinski negative. No troubles with the bladder or rectal sphincters. No fever but patient said he felt out of sorts just before illness. Physical examination of the rest of the body did not reveal anything abnormal. Previous history did not yield anything relevant to the illness. No evidence of dietetic insufficiency or peculiarity. Blood W.R. negative. C.S.F. no abnormality. Urine no abnormality. Patient showed steady and marked improvement on vitamin B<sub>1</sub> therapy. About 3 weeks later when he left, he could walk without support but was

a little shaky, had regained considerable power in arms, and sensory symptoms had greatly improved.

*Case 3.*—D., 35, M. M., an agricultural worker admitted on 26th May, 1942, was completely incapacitated with flaccid paralysis of all four extremities, wrist-drop and foot-drop, glove and stocking anaesthesia, and negative Babinski. Muscles tender and wasted. The paralysis came on 1½ months previously after a bath, with paræsthesia and muscular weakness spreading upwards from the legs and becoming extreme within a few days. Some disturbance of urination in earlier days. Physical examination of the other systems and previous history did not yield any relevant information. Blood W.R. negative. C.S.F. negative. Patient stayed only 5 days in hospital and subsequent course of the disease is unknown.

**Group II : Polyneuritis with acute onset and positive Wassermann reaction.**

*Case 4.*—V. J., 25, O. M., a house servant, was admitted on 14th February, 1942. Two months previously paræsthesia and weakness appeared in the hands and arms. Weakness gradually increased and became marked in a few days involving the muscles of the shoulder girdle and the trunk, the legs also weakened but compared with the arms retained considerable strength and patient on admission could stand and walk slowly but needed a little support. On admission the paralysis was of flaccid type with considerable wasting of the arms, and shoulder girdle muscles Babinski absent. Abdominal reflexes absent. Deep reflexes absent in arms, sluggish in legs. No sensory symptoms whatever. In earlier stages bladder control reported to be defective. Apart from syphilis 5 years previously history and examination of the body yielded no relevant information. Blood W.R. +++. C.S.F. no abnormality. Anti-syphilitic treatment given in the hospital.

On 29th April, 1942, when the patient was discharged, he had regained considerable power in his arms and could walk but was still weak.

*Case 5.*—B., 35, H. M., was admitted on 22nd September, 1942. Three months previously the patient after his bath felt pain in the loin. Tingling and weakness appeared in the legs and within a few days the legs, trunk and arms were paralysed with retention of urine. No sensory symptoms. Deep reflexes absent. Muscles of arms and legs wasted and paralysed. Recti weak. Babinski absent. Superficial abdominal reflexes sluggish. Bladder functioning normally. Except syphilis 4 years previously history and physical examination negative. Blood W.R. +++. C.S.F. no abnormality. Patient put on anti-syphilitic treatment. On 19th May, 1943, patient could use his arms and walk without help but still weak.

*Case 6.*—P. B., 40, H. M., was admitted on 6th December, 1941, with history of flaccid paralysis of legs spreading to trunk, arms and face within a few days and temporary bladder disturbance, duration of symptoms about 3 weeks. Marked pain and muscular tenderness and anaesthesia of upper and lower extremities of glove and stocking type. Babinski, tendon and abdominal reflexes absent. As recovery set in, an extensor plantar response (bilateral) appeared without exaggeration of deep reflexes. At this time it was noticed that the extensors of the toe had regained voluntary power, whereas the flexors were still paralysed, and the sole of the foot was hyperæsthetic. The positive Babinski therefore could not be taken as evidence of an upper motor neurone lesion (Monrad-Krohn, 1938). A true pyramidal inversion of the plantar reflex may also occur in acute febrile polyneuritis during the stage of convalescence (Cobb and Coggeshall, 1934). There was a history of syphilis several years previously, history and physical examination yielded no additional information. Blood W.R. +. C.S.F. no abnormality. Anti-syphilitic treatment was given. On 17th April, 1942, when the patient left hospital, he had recovered considerably the use of arms and legs, anaesthesia disappeared but some

dullness of sensation over the feet and some tenderness of the soles of the feet on pressure were still present.

**Group III : Chronic polyneuritis.**

In the same period the writer observed five cases of chronic polyneuritis which could be assigned to the following ætiological groups:—

1. Leprosy. One case. Nervous manifestations in both legs. Nerves thickened. No skin lesion.

2. Nutritional. Two cases. One patient was a Kashmiri, the other was from the Kangra district. Dysentery or diarrhoea, anaemia, oedema of the legs, and peripheral neuritis involving the legs were present in both.

3. Diabetes. One case. Only the legs were affected.

4. Typhoid fever. One case. Patient showed flaccid paralysis of legs, trunk and arms with dysarthria developing soon after an attack of fever lasting about 3 weeks. Initial weakness became steadily worse and paralysis was complete in about 8 weeks. Plantar reflex flexor. No sensory disturbance or bladder involvement. Duration of symptoms about 5 months. Wassermann reaction negative.

#### *Clinical features of group I*

1. Onset sudden, spread of paralysis rapid. In case 2 the patient was rendered almost completely helpless overnight. History of fatigue or exposure in cases 1 and 3:

2. Paralysis was of ascending type, beginning from the legs. All the three patients were almost completely helpless on examination. There was involvement of the trunk, but the respiratory and facial muscles showed no paralysis. Wasting was only noticed in case 3.

3. All cases showed paræsthesia. There was little loss of superficial sensation in case 1, and no muscular tenderness. Cases 2 and 3 showed greater sensory loss of peripheral distribution and marked muscular tenderness.

4. Deep reflexes absent; Babinski negative or flexor. Defective control of bladder in early stage in all cases; rectum affected in case 1 only.

5. Cases 1 and 2 showed rapid recovery with an average duration of illness of about 6 weeks. Case 3 was observed for a short period only, but it was apparently a more protracted case and was showing little evidence of improvement. There was no death.

6. No prodromal symptoms were noticed (or they were too slight to be noticed). Patients showed no constitutional disturbance or fever.

7. Cerebro-spinal fluid showed no abnormality; there was no increase in cell content or globulin. Quantitative estimation of protein was not done. The absence of hyper-albuminosis may be attributed to mildness of tissue reaction.

8. Blood Wassermann reaction negative.

9. All cases occurred in April and May.

### *Clinical features of group II*

The signs and symptoms were essentially similar to group I with the following differences :—

1. Both the onset and spread of paralysis were somewhat less acute.

2. Paralysis showed a descending tendency in case 4. The paralysis was not severe, and patient not so helpless, except in case 6 in which the patient was completely paralysed and in addition showed facial paralysis.

3. A preponderance of motor symptoms was noticeable in the group except in case 6.

4. All cases showed a protracted course extending over several months and the recovery was slow.

5. Blood Wassermann reaction was positive in all cases and there was a history of syphilis.

6. No special seasonal incidence was noticeable.

The clinical differences between the two groups are thus quantitative except for the positive Wassermann reaction and history of syphilis.

### *Clinical features of group III*

This group is characterized by a slow onset and chronic course of disease; paralyzes mild and limited in extent except in case 5 which showed extensive paralysis without sensory phenomena. In all the cases an aetiological factor could be recognized.

### *Discussion of clinical features of groups I and II*

The clinical picture of all varieties of polyneuritis is essentially the same, the differences being quantitative rather than qualitative.

*Clinical features of polyneuritis.*—The different aetiological varieties maintain a constant mode of onset and course, and can be divided into acute, sub-acute and chronic polyneuritis. Walshe (1941) describes two varieties of acute polyneuritis occurring in apparently healthy people, in whom no dietetic, toxic or infective factor can be discovered.

I. 'Acute febrile' or 'acute infective' polyneuritis.—Brain refers to an 'acute rheumatic polyneuritis' following exposure to cold, which probably also belongs to this group. The clinical description of this form of polyneuritis varies from author to author. An analysis of symptoms of 122 cases reported in literature by Fox and O'Connor (1942) is therefore instructive. According to these authors—

1. Prodromal symptoms such as coryza, aches and pains, gastro-intestinal disturbance appear in 31 per cent of cases.

2. Motor symptoms are constant and are often first to appear, including paralysis of extremities, disturbance of tendon reflexes and occasionally organic reflexes.

3. Sensory phenomena, pain, paræsthesia or anaesthesia occur in 50 per cent of cases.

4. Intercostal muscles and diaphragm are seldom involved.

5. Facial paralysis occurs in 35 per cent of cases.

6. Blood is normal, perhaps slight leucocytosis.

7. Cerebro-spinal fluid. Protein increased in 50 per cent of cases. Cell count normal.

8. Prognosis—mortality 20 per cent. Recovery takes on average 2 to 3 months.

According to Walshe the patient is intensely toxic and paralysis is sudden and widespread, involving the extremities, trunk, and usually the face; less often paralysis of chest and transient loss of control of the bladder. Sensory phenomena are variable, often slight. The essential feature is a relatively quick recovery in about 4 weeks, if the patient survives.

Brain (1940), although agreeing with the general description of the disease, remarks : 'In the most favourable cases the patient is not likely to be convalescent in less than 3 to 6 months.' According to this author, prodromata may be slight or absent and there may be no fever during the paralytic stage.

Cases in group I, on comparison with symptoms detailed above, show absence of prodromata, fever and toxic phenomena, respiratory and facial paralysis, and of hyper-albuminosis in cerebro-spinal fluid. They however possess the essential features of sudden and widespread paralysis tending to relatively quick recovery in the absence of a fatal issue, and may therefore be taken to represent a mild form of acute infective polyneuritis. The four cases reported by Fox and O'Connor (1942) show prodromata, hyper-albuminosis and quick recovery but little or no toxæmia during the paralytic stage.

II. *Acute polyneuritis of unknown aetiology.*—Under this heading Walshe (1940) describes a polyneuritis with motor and sensory symptoms, a rapid onset, but on the whole less acute and extensive paralysis as compared with the acute febrile variety; there is no fever or constitutional disturbance, and recovery is long delayed. The two cases reported by him took 9 months to recover. Cerebro-spinal fluid showed slight excess of proteins.

The clinical features of this variety of polyneuritis resemble those of cases included in group II, except that case 6 shows more extensive and severe paralysis rather like group I and cases 4 and 5 show purely motor symptoms. The essential feature—a paralysis of rapid onset with a protracted course of disease—is noticeable in all the reported cases in this group.

There may be some doubt with regard to the classification of case 3 in group I. This case has features which are common to both groups I and II. The acuteness of onset, severity of symptoms, seasonal incidence, and a negative Wassermann reaction have been the chief considerations in the classification of the case, because the clinical course of the case is not definitely known. Such difficulties are unavoidable in a disease with such marked variations in the clinical picture and course as is suggested by descriptions of the disease from different sources.

*Aetiology of polyneuritis.*—Cobb and Coggeshall (1934) mention over eighty causes divisible into four groups in the aetiology of polyneuritis—

(1) Virus infections. (2) Bacterial infections. (3) Deficiency or disorder of metabolism. (4) Chemical poisons. Such a multiplicity of causes indicates that the causes are imperfectly understood. It is not surprising that Walshe opines that not more than ten factors can be rightly incriminated. Walshe is of opinion that in spite of the diversity of causes in the main clinical varieties of polyneuritis—acute, sub-acute and chronic—there is an essential clinical and pathological uniformity, the difference being quantitative rather than qualitative. It is, therefore, possible that a single metabolic poison is produced in the body as a result of the different causes, and acts as a neural and myocardial poison. Such a poison is produced in beri-beri as a result of disturbed carbohydrate metabolism due to vitamin B<sub>1</sub> deficiency, but the nature of the poison is not known; it does not appear to be pyruvic acid. Whether a similar mechanism operates in other forms of polyneuritis due to vitamin B<sub>1</sub> deficiency it is impossible to say at this stage, but Walshe believes that the results of vitamin B<sub>1</sub> therapy at least do not support this hypothesis. In particular he finds it difficult to explain the acute forms of polyneuritis on the hypothesis of avitaminosis. Current opinion appears to be that vitamin B<sub>1</sub> deficiency plays an important rôle in the causation of chronic forms of polyneuritis such as beri-beri, chronic alcoholism, pregnancy, chronic disorders of the alimentary canal and possibly restricted diet.

In group III an ætiological factor is recognizable in all cases.

*Acute febrile polyneuritis* is believed to be due to a specific but unknown virus infection. The rapid onset of symptoms in apparently healthy people, without obvious dietetic or constitutional defects, the factors of fatigue and exposure which precede some cases, seasonal incidence, febrile and toxic manifestations, possible leucocytosis, favour the hypothesis of infection. In group I cases some of these features are present, and the absence of toxic manifestations can be attributed to infection with a virus of low toxicity, giving rise to a benign type of disease.

*Acute polyneuritis of unknown ætiology.*—Walshe does not attempt to assign a cause to this form of polyneuritis, but he does not favour the avitaminosis hypothesis. Cases in group II, which have been classified under this heading, have the common characteristic of a positive Wassermann reaction and a history of syphilis. In a population with a positive W.R. rate of 10 to 15 per cent this association may be a pure coincidence, but it seems to the writer to be a suspicious coincidence. Polyneuritis due to leprosy may be associated with a positive W.R., but it was ruled out on account of the absence of other clinical evidence of leprosy and the fact that leprosy is not known to cause an acute form of polyneuritis. Is the *Treponema pallidum* the dominant factor in

the causation of this group of cases? Text-books are silent or lukewarm on the subject of syphilitic polyneuritis. Some of the books refer to a polyneuritis complicating the secondary stage of syphilis as a rare phenomenon. Cobb and Coggeshall (1934) deny the existence of syphilitic polyneuritis. Drought (1940) describes an acute polyneuritis with slight sensory loss, which may complicate the secondary stage of syphilis. The cerebro-spinal fluid is normal and pupillary changes absent. He also records a case, reported by Macnamara, of 'Landry's paralysis' with purely motor symptoms 6 years after syphilitic infection, from which the patient recovered but subsequently succumbed to tabes. According to present conceptions, a purely motor ascending paralysis which tends to recover completely is a form of acute polyneuritis with purely motor symptoms, and cases 4 and 5 in group II show purely motor symptoms. The *Treponema pallidum* has a special affinity for the nervous system, and in tabes dorsalis it admittedly attacks the root portions of the peripheral nerves. Might it not, occasionally, attack the rest of the peripheral neurone? It appears to the writer, therefore, that the relationship of syphilis to group II cases cannot completely be denied. Unfortunately there is no reference to the venereal history of the two cases described by Walshe.

*Vitamin B<sub>1</sub> deficiency in acute polyneuritis.*—An obvious objection is that syphilitic infection is common, whereas syphilitic polyneuritis is rare (if the experience of the writer is taken as unusual). The same objection applies to acute febrile polyneuritis which, although a virus disease, is said to be rare. Other virus diseases are far more common. The writer believes that in the causation of both varieties of acute polyneuritis some cause other than organismal also operates, and in spite of the authoritative opinion of Walshe which deserves the greatest respect, the most likely factor is vitamin B<sub>1</sub> deficiency, or some poison due to it. Although no dietetic peculiarities were noticed in the reported cases, and the average Punjabi diet is said to be adequate in vitamin B<sub>1</sub>, and gross vitamin B<sub>1</sub> deficiency is a rare phenomenon in the Punjab (the writer is only stating what one is asked to believe), the existence of sub-clinical deficiency cannot be entirely ruled out. Williams and Spies (1938) remark: 'The American diet is one of the best in the world and yet many Americans lack an optimum diet for growth and full vigour. Careful study has convinced most students of the disease that sub-clinical forms of vitamin B<sub>1</sub> deficiency occur frequently.' If this is true of America, what about the Indian masses whose economic and educational standards, taken with the appalling frequency of malaria and bowel disease, tuberculosis and other infectious diseases, provide the most favourable conditions for vitamin deficiency? Such factors as unbalanced, mainly carbohydrate diet, inadequate intake, deficient

absorption, excessive requirements, and deficient utilization will frequently meet the eye of a careful observer. Given a sub-clinical B<sub>1</sub> deficiency, possibly associated with increased susceptibility to toxic and infective influences, a virus, *Treponema pallidum*, or an unknown toxin may attack a devitalized peripheral neurone giving rise to rapid and even sudden loss of function. This would also mean that acute polyneuritis should be more common in the tropics which, indeed, the experience of the writer seems to suggest. In the absence of B<sub>1</sub> deficiency, the virus or the treponema may not gain a foothold. On the other hand in beriberi, in which bacterial causes are not believed to operate, deficiency of vitamin B<sub>1</sub> may exist for months, even years, before chronic neuritic manifestations set in.

**Diagnosis of acute polyneuritis.**—From the clinical point of view, acute polyneuritis presents a diagnostic problem of some complexity because the symptoms are widespread involving apparently the cord and sometimes the cerebrum. The difficulty is partly due to a narrow conception of the pathology of the disease. If it is realized that the peripheral neurone extends from the grey matter of the central nervous system to the peripheral end-organs, and that the whole of it or only part of it may show the maximum incidence of pathological changes, the variation in symptoms and signs in different cases and the different permutations of sensory, motor and reflex phenomena will be easily understood. It should also be remembered that transitory peripheral symptoms may be met with in acute virus infections of the central nervous system such as poliomyelitis and encephalitis lethargica.

1. *Acute myelitis.*—It is characterized by sudden motor and sensory paralysis below a segmental level. The paralysis is flaccid in type but exaggerated reflexes and extensor plantar response soon make their appearance indicating a lesion of the upper motor neurone. Involvement of the bladder is of a more serious nature than in acute polyneuritis.

2. *Poliomyelitis.*—The paralysis is asymmetrical and inconstant, often maximal at onset and then receding. In other cases it may spread from below upwards. There is no sensory loss. Recovery is also irregular. Some of the muscles recover rapidly, others show permanent paralysis with great wasting.

In cases of acute polyneuritis with preponderant or purely motor symptoms the resemblance is more marked.

It may be remarked here that the so-called Landry's paralysis is not now considered a separate clinical entity. An acute paralysis of spreading type without sensory phenomena may be due to acute anterior poliomyelitis or acute infective polyneuritis with preponderant motor symptoms.

**Treatment.**—According to Walshe, vitamin B<sub>1</sub> therapy does not influence the course of acute

or chronic polyneuritis. He concludes that therapeutic results at least do not lend support to the vitamin B<sub>1</sub> deficiency theory of causation of polyneuritis. This is an observation from a great authority, and it cannot be treated lightly. Furthermore, in the acute form of polyneuritis the course of disease varies considerably from case to case, and it would be difficult to assess the value of a therapeutic measure unless a large number of cases were treated under properly controlled conditions. In the reported series of group I, cases 1 and 2 received intensive vitamin B<sub>1</sub> therapy at an early stage of the disease and both recovered rapidly. Case 3 did not receive this treatment and was in a protracted state of helplessness. It would be rash to draw conclusions from such a short series, but the results suggest the therapeutic utility of vitamin B<sub>1</sub> administered at an 'early' stage of the disease before structural changes have set in. On the other hand, the cases reported by Fox and O'Connor, which the writer considers comparable to this group, recovered without vitamin B<sub>1</sub> therapy in an even shorter period. In group II cases, anti-syphilitic treatment alone was administered. Vitamin B<sub>1</sub> could not be given and the course of improvement was slow but certain. In the protracted course, treponema infection may have been the principal factor. Whether the administration of vitamin B<sub>1</sub> to this group of cases would have hastened recovery it is impossible to say. What would have been the course of the disease without anti-syphilitic treatment it would be difficult to say without controlled observations on similar cases.

#### *Summary and conclusions*

1: Acute polyneuritis occurring in apparently healthy people in whom no toxic, infective or dietetic factors can be discovered is not an uncommon clinical experience. In the same period the writer observed as many as six cases of acute and only five cases of chronic polyneuritis.

2. The essential feature of acute infective polyneuritis is extensive paralysis of sudden onset from which the patient recovers rapidly if he does not succumb to the disease. Three cases of this type (group I) are described in the text, but the disease appears to be relatively benign, possibly due to infection with a virus of low virulence.

3. A less acute and milder form of polyneuritis with a protracted course and of unknown aetiology is described by Walshe. Three cases (group II), described in the text, belong to this variety. In the cases observed by the writer, however, syphilis appears to be one of the aetiological factors.

4. Vitamin B<sub>1</sub> deficiency is not believed to play a part in the direct causation of acute polyneuritis, but it has been suggested that sub-clinical deficiency may be a predisposing factor and a specific virus and *Treponema pallidum* precipitating factors. There may be



other unknown precipitating factors to explain such cases as those reported by Walshe.

5. The efficacy of vitamin B<sub>1</sub> therapy in polyneuritis, particularly in the acute forms, is open to considerable doubt, but the writer's experience suggests that it is worthy of further trial under controlled conditions.

6. In chronic polyneuritis an ætiological factor can usually be found. A reference to five cases observed in the same period (group III) has been made. Details of one case of polyneuritis, with no sensory loss, following typhoid fever are included.

7. Case 6 illustrates the presence in exceptional circumstances of extensor plantar response in peripheral paralysis.

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[Note.—The editor is interested in this subject partly because he himself in 1939 suffered from a very severe attack of acute polyneuritis following directly on a respiratory infection of 'influenzal' character. The paralyses were extensive, including the limbs, the face, the respiratory muscles and the glottis, and the treatment consisted in artificial respiration (Bragg-Paul), artificial feeding, and heroic doses of vitamin B<sub>1</sub>. Whether the latter had any effect it is impossible to say. Recovery took several months.—EDITOR, I. M. G.]

#### DETERMINATION OF BLOOD GROUPS FROM MEALS OF BLOOD-SUCKING INSECTS

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*The material.*—Mosquitoes and bed bugs were fed on subjects of known blood groups and squashed on chemically pure filter-paper. The stains so obtained were dried.

The insects were bred from eggs in the Entomological Department of the School of Tropical Medicine. The mosquitoes were fed once only

and then squashed, some after 3 hours and others after 24 hours. The bed bugs were fed for several days until a suitable size was reached. Then, like the first batch of mosquitoes, they were squashed 3 hours after a feed. The difference between the squashing in the two cases was accidental, not intentional or significant in any way.

*The method and results.*—The technique described by the writers for the determination of blood groups from stains was followed (Greval, Bhattacharji and Das, 1943). Briefly, (i) the MDESA (minimal dose of equal and simultaneous agglutination) of a serum ab (from a subject O) was determined—and found to be 1 in 16\*; (ii) 25 milligrams of the stained filter-paper were left in contact for half an hour at blood heat and overnight at ice-box temperature with 0.1 c.c. of the serum dilution containing 3 MDESA in a unit volume—3 in 16 dilution, and (iii) the serum dilution after contact was removed by centrifuging, and was tested with 2 per cent suspensions of known rbc A and rbc B for the loss of isonins a and b.

The serum dilution absorbed with the stain obtained by squashing a mosquito fed on subject A had lost a; the dilution absorbed with the stain obtained by squashing a mosquito fed on subject B had lost b; the dilution absorbed with the stain obtained by squashing a mosquito fed on subject AB had lost both a and b; and the dilution absorbed with the stain obtained by squashing a mosquito fed on subject O lost neither a nor b.

The stains obtained by squashing bed bugs were tested in the same way with the same results.

*Medico-legal implications.*—Mosquitoes and bed bugs may suck blood from a person of one blood group and on being squashed on articles of another person of another blood group may create a false evidence against the latter.

Insects are known to pass blood from the anus just after commencing a feed. The droplets so passed and deposited can be over a millimetre in diameter and give positive chemical, spectroscopical and serological tests. They may yield enough material for grouping tests to be done by those who pride themselves on getting results from microscopical quantities. For medico-legal purposes, however, such acts of supererogation (Sutherland, 1910) cannot be commended (Greval, 1940).

Professional keepers of leeches empty the latter, after application and engorgement, by pricking them near the posterior end and then milking. The blood of a certain group may thus drop accidentally or be squirted intentionally on the articles of another person of another group and again create a false evidence.

Even lice crushed between the thumb nails (the usual method of destruction in India) may

\*The volume remaining constant the dose is expressed by dilution.



leave the blood of a different group under the nails of a subject.

As an accused person cannot be compelled to give blood for grouping tests, the possibility of finding the blood in a mosquito caught in his mosquito-proof bedroom or in his mosquito net may be exploited. A well-engorged mosquito will yield enough stain for a test. It must of course be established that the insect has not sucked blood from any other source.

Incidentally, the blood groups in India are more evenly distributed than in Europe or America. Determination of group from stains is likely to furnish, therefore, more information.

Conveniently, the term 'insects' includes all blood-sucking 'vermin'. Attention has been drawn to them previously with reference to blood stains unconnected with deeds of violence (Greval, 1941).

#### Summary

1. Blood groups have been determined from the meals of mosquitoes and bed bugs.

2. Blood-sucking vermin may be responsible for causing blood stains unconnected with deeds of violence and yet be of groups different from those of the owners of the stained articles.

#### Acknowledgment

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### CHEMICAL METHOD OF OBTAINING DRY BLOOD PROTEINS FOR TRANSFUSION PURPOSES

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THE difficulties connected with the storage, preservation and transportation of plasma and serum in liquid form have led to the necessity of preparing these in dry form. Most blood banks are now drying these liquids by one or other of the various physical methods known (Dyer, Sankaran and Subrahmanyam, 1943). Elaborate machines have been constructed, such as the Desivae, Adetvae and others, for this purpose. These machines are not only costly

but also not easy to obtain in the present emergency. This naturally raises the question as to whether the proteins of the serum and plasma cannot be obtained in a dry form by the use of cheaper chemical methods. As long ago as 1910, Hardy and Gardiner made the observation that, by the addition of alcohol or acetone to serum or plasma at a temperature below 5°C., the serum proteins can be completely precipitated without denaturation, and the precipitate readily obtained in a dry form. Furthermore, they also showed that the temperature coefficient of denaturation of proteins by alcohol or acetone is of the order of 600 per 10°C. Basing our work on these observations, we elaborated the following method of preparing dry blood proteins from serum, and tested the value of the product for transfusion purposes.

*The method.*—Blood was collected into sterile bottles under aseptic precautions and stored immediately in a refrigerator till all the serum had separated (usually 24 to 48 hours). The serum was then drawn into sterile bottles and cooled to 0°C. and to this was added in a thin stream alcohol or acetone, previously cooled to 10°C., in the proportion of 9 of alcohol or acetone to 1 of serum. During this process, as the temperature of the mixture rises, precautions were taken to maintain the temperature at a low level by the use of a freezing mixture of ice and salt. The precipitated proteins were separated by the use of a covered Buchner funnel kept surrounded by freezing mixture. The precipitate was treated twice again as before with cold alcohol or acetone to remove all traces of moisture. The final precipitate was treated with cold ether to remove traces of alcohol or acetone. The ether-moist precipitate was spread in sterile petri dishes with an aseptic technique, and was exposed to a current of dry sterile air; later, the petri dishes were kept in a vacuum desiccator to ensure a perfectly dry product, i.e. with a moisture content below 1 per cent. When drying was complete, the product was transferred to sterile bottles. The product was a pearly-white powder readily soluble in distilled water and in normal saline.

*Results.*—By the above technique, several samples of serum proteins in dry form were prepared from (i) sheep's serum and (ii) human serum. The first product was tested on sheep in two ways: (i) for precipitin formation and (ii) for any toxic effect on transfusion. Repeated injections of the reconstituted serum proteins into sheep failed to induce precipitin formation; this fact shows that denaturation had not occurred. Transfusion of large amounts of the material into sheep also failed to produce any toxic manifestation.

The second product from human serum was reconstituted and transfused into an experimentally shocked cat according to the technique of Krishnan, Mukerji and Dutta (1944) and was found to be satisfactory. The rise in blood pressure was good and it was well maintained.

The experiments described above were commenced by the Blood Bank Research Unit at Calcutta early in 1942 and completed in April of the same year. In July 1942 after this work was completed, Reid and Bick (1942) reported that work on similar lines had been done by them and the 'Hardyized' proteins (as the product is now called) had given encouraging results in transfusion experiments on humans. These workers have also shown that Hardyized protein is free from certain pharmacological peculiarities met with in liquid serum and physically dried serum proteins. Although the number of samples prepared and tested by us is small, and the experiments confined to laboratory animals, in view of the very satisfactory results obtained even in our preliminary experiments, we felt that the results of our observations should be recorded. If this method is properly elaborated for large-scale production, we have no doubt that it will prove a good alternative method of obtaining dried human serum or plasma proteins for transfusion purposes in man. Particularly where the more expensive and elaborate machinery required for drying serum by physical methods is not available, this simpler and cheaper method may be given a trial.

#### Acknowledgment

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### PYROGENIC REACTIONS FOLLOWING INTRAVENOUS SALINE INFUSIONS

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By the use of rabbits, Seibert (1923) studied the nature of fever-producing substances found in distilled water, and was of the opinion that the rate of injection, contaminating substances from the Berkefeld candle, resistance and hypersensitiveness of individual animals, hemolysis, hydrogen-ion concentration, impurities such as

organic salts, glass dissolved from the container, gases from the air, and the constituents of the stopper were not the causes of the fever, but a filtrable product produced by a specific bacterium in distilled water. This was considered to be the cause of the pyrogenic reactions following intravenous injection in large quantities.

Williams and Swett (1922) claimed that when fluids with a higher or lower hydrogen-ion concentration than that of blood were injected into the circulation at a rate or in an amount that the blood cannot neutralize or buffer, reactions characterized by chill and prostration follow.

The present paper reports a study of these two rival theories.

Origin of the work: In order to render saline solutions used in cholera cases non-pyrogenic, Panja, Malik, Paul and Ghosh (1942) prepared hypertonic saline solutions in freshly prepared distilled water and observed that these did not produce any rigor or rise of temperature in cholera cases. It was concluded from these findings that the reactions were due to the pyrogenic substance alone as described by Seibert and others. Later, alkaline saline solutions, which are also extensively required in the treatment of cholera, were prepared in freshly prepared distilled water and injected intravenously into patients. There was sometimes a rigor and a rise of temperature, though less marked than when tap water which is alkaline in reaction was used. These findings encouraged the following experiments on rabbits and cholera cases.

Saline solutions were injected intravenously in 10 c.cm. amounts into healthy rabbits; and in 1 pint doses into cholera cases and the pyrogenic effects were studied under the following heads:—

(a) The rectal temperature was recorded before and after the injections every 15 minutes for 2 hours. The variation in temperature was the difference between the temperature immediately before and the highest attained after the injection during this period of 2 hours.

(b) The presence of 'pyrogenic substance' as described by Carter (1930) was demonstrated, and the amount was estimated by potassium permanganate and ammonium oxalate titration in these saline solutions.

(c) The pH of these solutions was determined by Hellige indicators.

The following saline solutions were used in the experiment:—

(1) Hypertonic saline solution—140 grains of sodium chloride in 1 pint of tap water.

(2) Hypertonic saline solution made with 140 grains of sodium chloride in 1 pint of freshly prepared distilled water.

(3) Alkaline normal saline solution—90 grains of sodium chloride and 90 grains of sodium bicarbonate in 1 pint of tap water.

(4) Alkaline normal saline solution made with 90 grains of sodium chloride and 90 grains of sodium bicarbonate in 1 pint of distilled water.

(5) Hypertonic saline solution—140 grains of sodium chloride in 1 pint of tap water—pH adjusted to 7.1 with dilute sulphuric acid.

(6) Hypertonic saline solution—140 grains of sodium chloride in 1 pint of tap water treated with acid potassium permanganate to oxidize the organic matter present, and pH adjusted to 7.1.

(7) Acid normal saline solution prepared with 90 grains of sodium chloride in freshly prepared distilled water and the pH adjusted to 5.3 with dilute sulphuric acid.

E. Merck's sodium chloride and sodium bicarbonate were used in the experiments.

The results are shown in the following tables:—

*Table showing the results in rabbits*

Serial number	Materials	Number of animals used	Average normal temperature of these animals	Average normal variation of these animals	Average temperature at the time of injection	Average maximum temperature after the injection within 2 hours	Average variation between the temperatures before and after injection	Actual variation due to injection	Average pH of the injectable substances	Average amount of oxygen consumed by the organic matter present in 100 c.cm. of water
1	Hypertonic saline solution in tap water.	10	102.47	0.26	102.36	104.3	1.94	1.68	8.5	0.25 mg.
2	Hypertonic saline solution in distilled water.	14	103.00	0.4	103.00	103.4	0.4	0.0	7.1	nil
3	Alkaline normal saline solution in tap water.	10	102.23	0.36	102.1	104.4	2.34	1.98	10.2	0.25 mg.
4	Alkaline normal saline solution in distilled water.	15	103.05	0.33	102.95	104.03	1.08	0.75	9.1	nil
5	Hypertonic saline solution in tap water. adjusted to pH 7.1.	10	101.93	0.24	102.1	103.8	0.93	0.74	7.1	0.25 mg.
6	Hypertonic saline solution in tap water treated with potassium permanganate and pH adjusted.	10	102.4	0.56	102.6	102.7	0.14	0.0	7.1	nil
7	Acid normal saline solution in distilled water.	12	102.34	0.12	102.4	103.27	0.87	0.75	5.2	nil

*Table showing the results in cholera cases*

Serial number	Materials	Number of cases	Average temperature before injection	Average maximum temperature after injection	Average variation of temperature	Rigor	pH	Average amount of oxygen consumed to oxidize the organic matter present in tap water
1	Hypertonic saline solution in tap water.	7	96.0°	103.0°	7.0°	+	8.5	0.25 mg.
2	Hypertonic saline solution in distilled water.	6	97.4°	98.4°	1.0°	—	7.0	nil
3	Alkaline normal saline solution in tap water.	6	96.5°	102.8°	6.3°	+	9.5	0.25 mg.
4	Alkaline normal saline solution in distilled water.	33	96.9°	100.6°	3.7°	+	9.1	nil
5	Hypertonic saline solution in tap water adjusted to pH 7.1.	7	98.5°	102.0°	3.5°	+	7.1	0.25 mg.
6	Hypertonic saline solution in tap water treated with potassium permanganate and pH adjusted.	20	99.4°	99.8°	1.4°	—	7.1	nil

From the results tabulated above it appears—

1. That the use of freshly prepared distilled or 'pyrogen-free' water for making the solutions reduced the pyrogenic reactions of the injection even in solutions of low or high pH.

2. That the use of acid or alkaline solutions, even if made with pyrogen-free or freshly distilled water, is followed by some rise of temperature.

### Conclusions

A rise in temperature after injection is seen (a) when pyrogen-free water is not used or (b) when the solution injected is either more acid or alkaline than that which blood can neutralize or buffer. When neither of the factors is present, there is no rise of temperature.

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## TALIPES EQUINO-VARUS\*

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### Introduction

We have not been able to find any figures on the incidence of clubfoot in India as compared with other countries. But the condition is certainly common enough that every practitioner may be called upon sooner or later to advise and give his opinion on the line of treatment to be followed, in at least one case. We have for some years been interested in clubfoot, and in our hospital practice in Gujarat have had the opportunity of seeing and treating a large number of cases. Judging from the series of cases seen, two points seem obvious. Firstly, the average general practitioner does not advise the parents of children with clubfoot seen by him to get immediate treatment by some competent surgeon; some actually advise the parents of the child to wait till it is older. Secondly, a rather large number seen by us have had previous treatment elsewhere; plaster, operations, etc., with very poor results. These facts, together with the information gained from contacts with physicians and surgeons in other parts of India, would indicate that most methods followed in the treatment of clubfoot do not give satisfactory results.

While discussing these problems some years ago on board ship with an Australian surgeon recently from London, I was advised by my friend to communicate with Denis Browne, F.R.C.S., one of London's leading orthopaedic

surgeons, who had some new ideas on the treatment of clubfoot. After having obtained rather indifferent and unsatisfactory results with all of the older, out-of-date though standard methods of treating clubfoot, we were only too glad to get these newer ideas, which incidentally are especially suitable for India where so many of the children brought to us are older, and many old enough to walk, or even walking.

Except for the use of adhesive plaster, which I advocate for reasons which I will give later, the following paper follows the teaching of Denis Browne.

### Pathology

Talipes equino-varus belongs to a group of deformities which develop *in utero* from an abnormal pressure, resulting in an abnormal moulding of the foot. Of the group of 'moulding deformities', those of the foot are commonest, as the foot can be more easily displaced than any other part of the child's body. Owing to their stiffness and irregular shape, the feet do not as easily conform to the shape of the uterine cavity as do the hands. This deformity of the feet may take two forms:—

(a) *Calcaneus* from pressure on the soles of the feet in the normal folded-leg position of the child *in utero* is the commonest. Normally, the new-born child's feet show a certain amount of calcaneus.

(b) *Longitudinal bending of the foot* may occur in the same folded-leg position, when the feet turn inwards taking the uterine wall pressure on their outer borders instead of the soles. Talipes equino-varus belongs to this group of deformities.

### *The true nature of the deformity called talipes equino-varus*

The foot when it is in the folded-leg position is turned inward under the pressure of the uterine wall and may show a series of deformities depending on the degree of increase in pressure.

Firstly, with a slight increase in pressure, the forepart of the foot alone meets the moulding force and bends inward. This is known as 'metatarsal varus'. (Browne considers this term as confusing, as it attempts to describe deformities in terms of normal movements of joints, which in this case does not apply, as the sole of the foot remains horizontal so that there is no varus in the ordinary sense.)

Secondly, with a further increase in pressure, the whole foot is moulded to conform to the shape of the uterine cavity, the heel bending inwards behind the fixed point of the ankle joint. In addition, the increased pressure swings the whole foot into varus, and, because of the inclinations of the joint surfaces, into an equinus also. (The classical description of equino-varus ignores the actual bending deformity.)

Thirdly, in the final and greatest degree of pressure, the bending of the foot is so great that the forepart of the foot is bent to a point where

\* Being a paper read at the All-India Medical Conference, Ahmedabad.

the big toe points straight upwards along the tibia. In this case, equinus completely disappears and the deformity is described as 'extreme varus'.

In all three of the above degrees of deformity, there is no twisting of the leg bones. The muscles atrophy from immobilization, and are unbalanced owing to the over-stretching of the peronei and extensors, while the stronger opposing groups are left in a contracted state. There is no true paralysis of the muscles.

A single clubfoot is never very severe; since if one foot is normal, there cannot have been a very high uterine pressure. If, however, there is a double deformity, both feet are more apt to be deformed to a greater degree than a single clubfoot; and furthermore, usually one foot is more severely deformed than the other. (This is the foot that is the outer one in the cross leg position.)

#### *Rejected teaching on the causes of clubfoot*

Browne rejects the following as possible causes of clubfoot:—

Nervous causation, arrested development, hydraulic pressure, defective germ plasm, and congenital dislocation of the astragalo-scapoid joint.

#### *Treatment*

*Aims of treatment.*—The important thing in correcting the structural defect of the foot is to get the forefoot naturally used and held at a correct angle to the body; that is, pointing outwards about 20 degrees in relation to the sagittal plane of the body as a whole. In addition there must be a full range of movements of the joints. The inward bending of the heel will automatically adjust itself if the forefoot is used correctly. To overcome the muscle imbalance, it is necessary that whatever method is used in holding the position of the forefoot should also permit the use of the leg and ankle. It is of the utmost importance that, whatever form of treatment is used, there should be a simultaneous correction of structure and function.

#### *Method of treatment*

(1) *Correcting the longitudinal bend* of the foot may be done by the hands alone on a child less than two years of age. In a child over two years of age, some mechanical device will be required, as the strength of the hands will be found insufficient. Browne suggests the use of a wood-worker's vice fixed to the end of the operating table by a ball and socket joint.

On one side of the vice a block of wood is fixed with a notch cut in it so that the two edges act as points of pressure; between these two points in the opposite direction presses the apex of a wedge-shaped prominence on a similar block on the other side. The foot is placed between these two blocks, with the single point pressing on the apex of the longitudinal curve just in front of the external malleolus where

the bone is strongest, and its concave inner border opposite the concavity of the notch in the other block. When the vice is screwed up, the deformity is reversed by forcing the foot into the notch so that it has a longitudinal bend, convex inwards instead of outwards.

The method we use to correct the longitudinal bend of the foot, in cases where it cannot be done by the hands alone, is to make use of an empty anaesthetic drop bottle (such as is used for chloroform) to act as a fulcrum. The bottle is laid on its side on the table and covered with a piece of cotton-wool. Now the apex of the longitudinal curve of the deformity just in front of the external malleolus is applied to the bottle. Then with the palm of one hand applied to the forefoot and the other palm applied to the inner aspect of the ankle joint, heavy pressure is brought to bear on these two points by the operator swinging the full weight of his body down through his extended arms and forcing the deformity into a reversed position.

(2) The second step in the treatment is to gain the *full normal movement* of the joints involved. This is done by forcing the forefoot up into full calcaneo-valgus; that is, the dorsum of the foot is forced up back against the anterior surface of the leg. The object is to carry this correction to a point where the little toe can be made to touch the leg. This correction again is best accomplished by the hands up to limits of their strength. To get the full force applied correctly, the palm of the hand should be applied to the sole of the foot, with the forefingers curled behind and gripping the back of the child's ankle.

When the foot is too stiff for this to be done with the hands alone, Browne suggests the use of an apparatus somewhat like a large pair of nutcrackers. The one essential mechanical point is that the axes of the hinge joint which connects the two limbs of the 'crackers' must coincide with the axes of the ankle joint. The limbs of this 'nutcracker' may be made of teak boards. The hinge consists of two pairs of bolts joined together by eyes at their ends. By means of the butterfly nuts on the bolts, it is possible to control the position of the hinges and the inclination of the boards to each other to suit different cases. In lieu of such an apparatus we place the patient on a low table with a stiff support such as a small wooden platform raised about two inches, under the leg, leaving the ankle and forefoot free, hanging over its edge. With the left hand the ankle is grasped and held down on to the hard support beneath it. The palm of the right hand is applied to the sole of the foot and the right shoulder of the operator brought down against the hand with the full weight of the operator's body behind it, forcing the foot back and up into full calcaneo-valgus.

(3) Thirdly, after the deformity has been corrected and the joints forced through their normal range of movements, the *normal bending out of the foot in relation to the sagittal plane*



of the body at about 20 degrees must be maintained by a suitable splinting.

#### *Method of splinting*

It is necessary that whatever device maintains the position of the forefoot should also permit of the foot being used. Such a device or method will favour the development of atrophied muscles and a correction of the muscle imbalance, by permitting the use of the muscles with the foot held in the correct position. Here in India where so many of the cases are seen after the child is several months old, and in some cases when the child is on the point of walking or even making attempts to walk, we have found the proper use of adhesive plaster an excellent method. Browne does not favour the use of adhesive plaster, as by its use he states that it is impossible to maintain the proper 20-degree out position of the forefoot in relation to the body as a whole. We disagree with this, and have found that, if adhesive plaster is correctly applied, the correct position may be maintained; and, furthermore, in an older child, the correct movements of the foot and the development of the atrophied muscles are favoured if the child is able to walk while its feet are in adhesive plaster bandages. Other methods of maintaining the correct position, such as plaster of paris, do not permit this. Browne has developed a light aluminium splint consisting of foot-pieces made by cutting out L-shaped pieces of 14-gauge hard aluminium, and bending out on one side to clear the external malleolus while bearing against the outer side of the leg. These foot-pieces may be fixed, by friction joints to an aluminium cross bar, at any desired angle in relation to each other. This splint is used up to the age of nine months, with fortnightly changes and manipulations. The feet, after correction, are fixed in the foot-pieces with adhesive plaster. The babies are encouraged to kick and to stand up in the splint as much as possible. After nine months, the aluminium foot-pieces are changed for a pair of boots which are riveted to a metal sole piece, which can be clamped to the cross bar. We have used this splint and have found it fairly satisfactory in early cases. The greatest difficulty in the use of this splint however, in most cases, is the mother of the child. Most mothers, in Gujarat at least, object rather strenuously to having the child's foot strapped and bolted to such a splint.

In brief, our line of treatment for a new club-foot case is as follows: The correction of the deformity is done carefully but completely the first time under a general anaesthesia (chloroform). In some cases the correction of the deformity may require considerable force, but if this force is carefully applied to the right points, except for a temporary swelling of the feet there is no untoward effect. After the deformity of the forefoot has been corrected, and the normal action of the joints has been obtained by manipulation, the foot is held by

adhesive plaster in an everted, adducted position, with a slight degree of valgus. This is accomplished by applying two strips of adhesive plaster (approximately three-quarters of an inch wide for a small child to one inch wide for an older child, and long enough to reach up to the knee). These strips are applied as follows: One end of the first strip is applied across the dorsum of the foot commencing opposite the base of the little toe. This is carried across the dorsum of the foot around the base of the big toe and then down and across the bottom of the foot to the outer edge of the forefoot. The foot is now held in the correct position as described above, while the other end of the strip is carried up and applied to the outer surface of the leg ending at a point just behind the head of the fibula. The second strip is now applied to the foot exactly over the first strip but the long free end is applied to the outer surface of the leg ending just in front of the head of the fibula. The foot is then bandaged firmly but lightly with a gauze roller bandage, commencing from just behind the toes around the forefoot, and proceeding up the ankle and the leg to a point below the knee. This bandaging prevents the sticking plaster from slipping. With reference to the type of adhesive plaster to be used, till recently we have always used the ordinary non-elastic type; but due to the present war-time conditions, for some months we have been forced to use elastoplast which is an elastic sticking plaster. This elastoplast we have found to be actually better than the old non-elastic type; but care must be taken that it is not drawn too tightly, as it may cause a pressure sore on the outer edge of the forefoot. (If a pressure sore does occur, the ulcer is dressed with some healing ointment or antiseptic powder for a week without applying adhesive plaster.) For the first four days after the above treatment, the child is kept in the hospital for observation.

Sedatives may be required in suitable doses to keep the child comfortable during the first day. After four days the bandages are removed and the foot is again manipulated; that is, forced round into full calcaneo-valgus. Adhesive strips and bandages are again applied in the same manner as first described. The child is then sent home and the parents are instructed to come at intervals of 7 to 15 days, depending on the distance they live from the hospital. (Some of our patients come from as far as 200 miles every 10 to 15 days for the necessary manipulation and bandaging.) On each return the old bandage is removed, the foot is put into full calcaneo-valgus and a new bandage is applied. The above method will usually give a satisfactory correction in three months for a child seen during the first month after birth. For older children, a series of manipulations over a period of from 6 to 18 months may be required to get the desired results. In each case, after the foot is considered to be in a satisfactory condition, the parents are advised to return for a check at



monthly or longer intervals, especially during the period when the child is commencing to walk.

#### *Rejected factors in treatment*

We agree with Denis Browne in rejecting the following factors in other methods of treatment :—

(1) The conception of the *normal position of the foot* being that of pointing directly forwards. The normal position should be considered as one with the foot at an angle of 20 degrees outward from the sagittal plane of the body. If this position is not obtained and if the correction of the foot is only carried to the point where the foot is pointing directly forward, there is much more likelihood of a relapse.

(2) The use of the term 'over-correction'. This is a wrongly used term as the foot is put in a position which its joints can compass normally. The correct term would indicate reversing a position or a deformity rather than over-correcting it.

(3) *The Thomas wrench*.—'On the elements of talipes deformity it is most efficient on the least important, the varus; it is less efficient on the equinus; and least efficient of all on the primary curve of the foot'.

(4) *Tenotomies*.—In most cases eventually a tenotomy results in more damage than good. The muscles, cut off from their insertions, shrink and degenerate permanently. The extravasated blood between the separated ends of the tendon forms contracting scar tissue making the final correction more difficult. It is a temptation to do a tenotomy because of the resulting ease with which it is possible immediately to force the foot into the required position. Browne lists a tenotomy on a clubfoot as one of the 'worst of surgical crimes'.

(5) *Open operation*.—Open operations are unnecessary except possibly to undo the results of previous open operations. Most open operations on cases of clubfoot only result in a stiffening of the foot and a wasting of the leg muscles, with no effect in increasing the range of movements of joints in the way that manipulations do.

(6) *Plaster of paris* gives complete immobilization, which is the last thing wanted.

(7) *Clubfoot shoes*.—These, unless used in connection with a cross bar, so that the position of one foot can be controlled by the other in relation to the sagittal plane of the body, often fail.

(8) *Grip on the bent knee*.—The commonest way of turning the clubfoot outward is the use of the bent knee as the point of purchase. The disadvantages are, however; the putting out of action of the muscles, and a tendency to produce knock-knees by stretching the internal lateral ligament of the knee.

#### *What results may be expected*

We believe that the method described above for treating clubfoot will give better results than

any of the older standard methods. Any results must be judged on the resulting suppleness of the foot and the muscular development of the calf. The surgeon's difficulties vary with the degree of moulding of the foot in any given case. However, any patient suffering from a true equino-varus, and in whom the foot has not been twisted up and is beyond the horizontal, and who is brought for treatment soon after birth, should be permanently cured by the time the patient can walk.

Previous treatment may render a good result impossible. If the foot has been immobilized in plaster, the original wasting of the calf muscle will be greatly increased; if a tendon has been cut, the ankle will be stiff; an open operation means that the child will be in the permanently crippled class.

#### *Conclusion*

Three points are covered in the above paper :—

(1) Acceptance of the compression hypothesis of the cause of talipes, which is one of a group of congenital deformities. This acceptance gives us an explanation for the variations of structure and function in this deformity; and thus a basis on which to carry out a rational line of treatment.

(2) The essential principle in treatment is that structure and function should be corrected simultaneously.

(3) A method of using adhesive plaster is described to hold the foot in the correct position, and at the same time permit of its use. This we consider the method of choice in India because of the older age at which the average case of clubfoot is seen.

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#### VITAMIN B DEFICIENCY STATES AMONG WOMEN IN MYSORE

(A SURVEY OF CASES ADMITTED INTO FEMALE MEDICAL WARDS, KRISHNARAJENDRA HOSPITAL, MYSORE, DURING 1943)

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*Introduction*.—Vitamin deficiency states hold the centre of the stage to-day as indicated by the innumerable papers which are published from time to time in the medical periodicals. The present war, on account of its unavoidable demands on our restricted food supply, is responsible in a great measure to the urgency of the problem. This paper is the outcome of observations made in the female medical wards of the Krishnarajendra Hospital, Mysore,

during the year 1943, and is an attempt at assessing the incidence of vitamin B complex deficiency states and their clinical manifestations.

*Incidence.*—There were 826 admissions into the wards between 15th January, 1943, and 22nd December, 1943. Out of these admissions, 78 women presented signs and symptoms of vitamin B deficiency. Very few among these 78 women presented a clear-cut single vitamin deficiency state as described in the textbooks, and the majority of them suffered from sub-clinical deficiency states rather than a fully developed clinical condition. Both these points have been referred to in the editorial of the August number of *The Indian Medical Gazette* (1943). A third important aspect is that, as compared with the 78 cases presenting signs and symptoms of vitamin B complex deficiency, there were only 7 cases manifesting signs and symptoms of the deficiencies of either A, C or D, a point which will be again referred to.

It is now known that the vitamin B complex is composed of at least four separate components which have some influence on human metabolism and whose lack in food results in definite clinical states (Sebrell, 1941). Beri-beri is due to deficiency of B<sub>1</sub> component. The B<sub>2</sub> component is more complex. There is a certain amount of confusion even now about the terminology of the several sub-groups of the B<sub>2</sub> component, and the last word has not been written about them. Three of the several parts belonging to the B<sub>2</sub> complex have been isolated in a pure state and prepared synthetically, and the clinical manifestations of their deficiency elaborately studied. First is the human-pellagra-preventive factor, now identified mainly as nicotinic acid. Its deficiency is the main cause of pellagra in human beings. Riboflavin is another component and its deficiency results in cheilosis, angular stomatitis, a certain type of glossitis, sealy dermatitis and superficial keratitis (Swaminathan, 1942). The third component has been identified as pyridoxine, a deficiency of which leads to a syndrome simulating paralysis agitans and difficulty in walking (Sebrell, 1941). The above deficiency states do not usually appear singly as has been mentioned before. There is a certain amount of overlapping of the several deficiency states in the same person, symptoms of deficiency of one among them being predominant over the rest, an observation pointed to by Giri (1942).

The complaints of our patients conformed in the main to the symptomatology usually described in connection with vitamin B lack. These were: gastro-intestinal disorders ranging from anorexia to chronic diarrhoea; skin conditions varying from sealy dry skin over the exposed parts of the body such as the face, hands and feet, to exfoliative and bullous dermatitis; tongue changes varying from small areas of ulceration to typical atrophic glossitis; symptoms of cardiac insufficiency ranging from simple breathlessness on exertion to oedema and orthop-

noea; nervous manifestations ranging from subjective symptoms such as numbness or pains in the muscles of the extremities to ataxia; mental changes varying from depression, irritability, confusion, loss of memory to extreme nervousness, delusions of persecution and dementia. In my series of cases, 52 had some digestive disorder, 47 had anaemia, 33 had tongue changes (the majority being cases of atrophic glossitis), 2 had cheilosis, 3 angular stomatitis, 14 had oedema of the feet, 2 had symptoms of peripheral neuritis, 10 had dermal changes, 4 had smoky conjunctivæ (in two of whom there was circumcorneal vascularization), and 8 some type of mental disturbance. To ascribe the smoky condition of the conjunctivæ to vitamin B lack may not be justifiable, for we know that vitamin A deficiency manifests itself as xerophthalmia, and, when this change is still in the early stages and definite Bitot's spots have not formed, the conjunctiva appears dusky, simulating a condition of riboflavin deficiency. Attention has been drawn to this matter by Spies *et al.* (1939). Perhaps both vitamin A lack and B deficiency are operating to produce the eye condition. A similar difficulty has to be confronted when dermal changes are present and their causation has to be determined. Hyperkeratinization of the skin and phrynoderma are manifestations of vitamin A deficiency. In pellagra the exposed areas of the body surface present roughening, exfoliation and bullous formation in the skin. The roughening of the skin simulates vitamin A lack. The diagnosis in such conditions has to be made only on the basis of therapeutic response. In my series of cases, the dermal changes have been assumed to be due to B complex deficiency, as all of them responded satisfactorily to administration of vitamin B.

All except two of the fourteen patients who had oedema of the feet had suffered from chronic diarrhoea, and eight of them had superficial glossitis. Two complained of neuritic pains in the limbs and none had any demonstrable sensory changes except slight delayed sensation to cotton-wool over the feet only.

It is difficult to explain the causation of oedema. The oedema may be due to changes in the heart or peripheral vascular system, or in the blood or in the tissue fluids. The oedema cannot therefore be ascribed to lack of B<sub>1</sub> only, as many other factors are concerned in its causation, and as the response to only B<sub>1</sub> therapy was not found to be satisfactory. In fact a high protein diet and nicotinic acid had to be given in addition to B<sub>1</sub> to effect improvement. This finding is in conformity with that obtained by Ahmed (1942).

The anaemia in all the 47 cases was of the hypochromic, microcytic type, and in none of them the hyperchromic variety was found, though Ahmed mentions that rarely the latter type of anaemia is found associated with B complex deficiency states.

Of the eight patients in which some type of mental disturbance was demonstrable, two were

suffering from irregular pyrexia as a result of an urinary tract infection, *E. coli* having been found when a culture of a catheterized specimen of their urine was made. In the other six cases no other cause except some symptoms associated with vitamin B lack could be found to explain the mental condition. Four of the six patients gave a history of long standing diarrhoea, and these patients showed pellagroid changes in the skin with superficial glossitis. In two, no abnormality was demonstrable in any system except the mental disorder. One suffered from acute depression with a tendency to commit suicide, and the other would not talk or take any food until nicotinic acid therapy was instituted. Six of the eight patients having mental symptoms gave a history of a recent confinement and were treated as 'puerperal mania' outside without any improvement before admission into the Krishnarajendra Hospital. The dramatic improvement under nicotinic acid therapy established that they were mainly due to a B<sub>2</sub> deficiency state, a fact which has been definitely established by various workers such as Cleckley *et al.* (1939), Jolliffe *et al.* (1940) and Slater (1942). In fact, Cleckley *et al.* have come to the conclusion that many patients are allowed to die because of failure to recognize the cerebral symptoms of pellagra when other evidences of the disease are absent, and that a therapeutic test with nicotinic acid is justified in unexplained cases of hebétude or unconsciousness.

Attention should be here drawn to an important aspect of this deficiency state, and that is its great incidence among women who are in the child-bearing age and have recently delivered. In my series of cases, there were 10 patients below 10 years, 15 between 10 and 20 years, 23 between 20 and 30 years, 16 between 30 and 40 years, 6 between 40 and 50 years, 5 between 50 and 60 years and 3 above 60 years. About 50 of these women were in the child-bearing age, and 38 of these gave a history of having been delivered from a month to six months before. A reference has been made by the editor of *The Indian Medical Gazette* (August 1943) to the fact that the vitamins A and B deficiency is more common in India than deficiency of C and D and that the majority of the patients who had B complex deficiency were women. The impression created in my mind is that B deficiency states are the most common among all the vitamin deficiencies, and that the victims are usually women of child-bearing age. The condition has been precipitated in them by the demands made on their nutritive state by pregnancy, delivery and lactation, especially as most of them are subsisting on a borderline state of nutrition. This observation is not quite in accord with the findings of Clarke and Prescott (1943) who mention that B deficiency states were most commonly in women above 50, the average age being 53.

A deficiency state is brought about by (a) an inadequate intake of proper food, (b) a normal

intake during periods of stress and strain when the supply cannot meet the greater demand, and (c) by inadequate utilization due to faulty absorption or increased excretion brought about by disease of the gastro-intestinal tract. The periods of pregnancy and lactation being periods of nutritional stress and strain, the demand for vitamin B is naturally very great. If this demand is not met, and if a further pathological state such as hyperemesis gravidarum were unfortunately to be superimposed, a definite deficiency state would probably become established.

Until now, main emphasis has been laid on the adequate administration of vitamins A, C and D to pregnant women to prepare them for a safe confinement. Mention has been made of the administration of vitamin B<sub>1</sub> in the polyneuritis of pregnancy, and of the occurrence of riboflavin and niacin deficiencies in pregnant women attending the antenatal clinics in America by Ebbs (1943). The question is most important to South Indians, mostly subsisting on a carbohydrate vegetarian diet. An adequate supply of vitamin B is very important in these people, as this substance is required for the proper combustion and utilization of their carbohydrate diet. In addition to this, vitamin B being water soluble is not stored in the system, and any lack of this is quickly manifested clinically, according to Clarke and Prescott (1943), three months before the manifestations of lack of vitamin A, C, D or K could be recognized. This idea would explain the preponderance of vitamin B lack over that of A, C or D in my series of cases.

These facts show how necessary it is to give adequate amounts of vitamins B as well as A, C and D to pregnant women, and to keep the supply up during the period of lactation, the essential factor being administered in the shape of foods rich in B complex, or of concentrated extracts when suitable foods are not available.

The diet of the patients under consideration had been monotonously similar before their admission into the hospital. Almost all of them came from poor agricultural classes from the villages, and were living on rice gruel, ragi ball and buttermilk, with only occasional meat feeds. None of them were taking either maize or cholam. It would therefore appear that pellagroid states are not uncommon in non-maize eaters, an observation made already by workers such as Lowe (1931), Aykroyd and Swaminathan (1940) and Ahmed (1942).

The relationship between avitaminosis and urinary tract infection appears to be more than casual, and deserves an elaborate investigation. It looks as though they are closely associated. We know that diarrhoea is a common symptom of vitamin B deficiency, being the commonest complaint in my series of cases. It is also well known that, in chronic diarrhoeic states, resistance to infection is greatly undermined and the saprophytic *E. coli* in the intestines assumes parasitic activities and infects the urinary tract;

causing conditions such as pyelitis. In my series of cases, six patients gave a history suggestive of a urinary tract infection, and *E. coli* was demonstrable on culture of a catheterized specimen of urine in all cases. In the paper by Heilig and Puttaiya (1943) on the incidence and clinical types of urinary tract infections, it has been mentioned that a good proportion of the cases displayed mental symptoms varying from depression to delirium. Two of my present series showed definitely abnormal mental states; one suffered from extreme nervousness and delusions of persecution, and the other from violent mania. It was noticed at the time of our observations on urinary tract infections that a few of the patients remained in a depressive state of mind even after the pyrexia had subsided and the general condition of the patient had improved. I thought that this phenomenon was due to the after-effects of sulphanilamide therapy which was adopted to combat the infection, but in cases where the drug was not administered, the mental state was ascribed to the neurasthenia usually described in connection with bladder infections. As the two cases referred to above improved remarkably when nicotinic acid was administered, could it have been that in these cases a nicotinic acid deficiency was the basis of the mental derangement? One of the cases which responded dramatically to nicotinic acid therapy gave a history of recent delivery and of having developed fever; she was subsequently treated as a case of 'puerperal sepsis' with sulphanilamide and glucose, and, incompletely recovered, was admitted into the Krishnarajendra Hospital. The other case was that of a lady who had suffered from chronic diarrhoea and had been treated for B complex deficiency as an in-patient for a month or so, and was discharged relieved of her complaint. Three months later her people brought her again to the hospital, this time with fever and acute mania. While sulphanilamide, glucose, luminal, paraldehyde and even morphine would not improve her mental condition, the daily administration of 50 mgm. of nicotinic acid parenterally for a fortnight made her at the end of the period reasonable, quiet and co-operative. It looks as though the urinary tract infection precipitated a deficiency state which was not apparent before the toxæmia set in, so that nicotinic acid had to be added to sulphanilamide therapy to cause the recovery to be complete.

The pathological examinations in the present series of cases were marked by the paucity of abnormal findings.

In about 50 per cent of the cases there was a hypochromic microcytic anaemia; 21 cases had mild albuminuria but the urine microscopy, blood urea, urine concentration test and fundi were normal in all these 21 cases. There was generally a tendency for hypotension, this being significant in 12 cases. Fractional test meals showed a tendency to hypochlorhydria while in 10 patients there was achlorhydria. One case had an arterio-sclerotic fundus and one showed optic atrophy. X-ray examination of the chest was normal in all cases except three, one presenting a prominent

aortic knob and two cases showing bilateral infiltrations of the lung, suggestive of Koch's infection. Sigmoidoscopic examination was done only on such cases as presented a symptomatology of ulcerative colitis, and only one case showed the presence of ulcerations, 12 inches above the anal margin. Lumbar puncture was done in all cases which presented mental changes, and the cerebrospinal fluid was subjected to examination. The cerebrospinal fluid was normal and did not appear to be under tension in any case. Removal of 10 c.cm. of the fluid did not result in any appreciable improvement in any of the cases. Blood examination for W.R. and K. & K. was negative in all cases, and the leucocyte count was found to be within normal limits. Six had positive urine cultures, and parasitic ova (round-worm ova in eight and ankylostoma ova in four) were found in 12 cases. Results of sedimentation tests and tuberculin tests were found variable. Blood protein and porphyrin in urine were not estimated as they have been found to have no direct relationship with the deficiency state by Slater (1942), and several other workers.

Pellagroid states are characterized by seasonal relapses, but only two of these patients have returned with a relapse. The details about one have already been given. The other was a destitute who returned to the hospital in a month or so having suffered a setback in her condition owing to starvation.

While it is true that an indiscriminate administration of vitamins is not only irrational from the therapeutic point of view, but also unwise (since vitamins cannot replace natural foods) and uneconomical according to the findings of the Council on Foods and Nutrition and the Council of Industrial Health (1942), I feel that sub-clinical states of vitamin deficiency, particularly of the B group, are very common in our women who subsist on a dangerously low intake of food, and that their prompt recognition and early treatment are most important.

*Summary.*—Eight hundred and twenty-six patients whose ages ranged between 10 and 60 were admitted into the female medical wards between 15th January, 1943, and 22nd December, 1943. Out of these, 78 patients presented symptoms of vitamin B deficiency, while only 7 had signs and symptoms of deficiencies of other vitamins. The diagnosis was confirmed by positive response to vitamin B therapy in all cases. Sub-clinical states were more common than well-defined clinical states. There was an overlapping of the deficiencies of the several components of the vitamin B complex. Recent delivery and urinary tract infections appear to have more than a casual relationship with vitamin deficiency states. Two cases have been quoted in which the manifestation of mental disturbances was precipitated by delivery and urinary tract infection, and which responded to nicotinic acid therapy dramatically, showing that the condition was due mainly to a deficiency of nicotinic acid which was precipitated by sepsis.

My grateful thanks are due to my Medical Officer, Dr. C. Krishnaswamy Rau, for his kind permission given to me to utilize and publish the clinical material and for the very valuable suggestions given during the preparation of this paper. I owe a debt of

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## PRIMARY PNEUMOCOCCAL SERO-FIBRINOUS PLEURISY

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### Introductory

PNEUMOCOCCAL pleurisy is almost always secondary to a focus of inflammation in the lung, but it may be primary. The exudate is usually purulent, with much fibrin, and the outlook is favourable. When pleurisy is the only local manifestation of the infection, it is said to be 'primary' or 'idiopathic'; when, however, it is discoverable due to propagation from a focus of inflammation in the neighbourhood of the pleura, or to metastatic deposition in the pleura of bacteria brought by the blood current from some distant focus of infection, it is said to be 'secondary'. We call the pleurisy 'primary' only when we cannot discover the mode of infection of the pleura.

The pneumococcus may be a cause of fibrinous, sero-fibrinous, or purulent pleurisy. It is a common factor in the fibrinous form, but it is a very rare cause of clear serous effusion. Certainly 80 per cent or more of all sero-fibrinous pleurisies have a tuberculous basis.

Of the non-tuberculous cases with a sero-fibrinous exudate, 5.2 per cent have been found due to the pneumococcus. These pleurisies are usually secondary to pneumococcal disease of the lung, although the failure to demonstrate this may sometimes seem to justify the term

'primary pneumococcal sero-fibrinous pleurisy' (Emerson, 1924).

### Case report

A Muslim male, aged 17, was admitted into the hospital with the complaint of pain in the right side of the chest, duration 10 days. The onset was insidious, and he never complained of cough, pyrexia or any other acute pulmonary symptoms.

*On examination.*—The patient was afebrile but thin and pale. He had a pulse rate of 76 and respiration rate of 28 per minute, and his blood pressure was 104/78. Respiratory system: on the right side (from the back) the base showed diminished movement, diminished vocal fremitus, dullness, poor breath sounds of vesicular character, no adventitious sounds, and diminished vocal resonance. Other zones of the right lung and the left lung showed no abnormality. The 'sternomastoid sign' (Trail, 1943) was negative. Heart: the apex beat was in the normal position. No organic damage of the heart could be detected. Other systems were normal. A diagnostic paracentesis thoracis was done and clear, sero-fibrinous fluid was drawn out. A clinical diagnosis of tuberculous pleurisy with effusion was made, but a large amount of fibrinous deposit in the fluid suggested the possibility of pneumococcal pleurisy.

*Investigations.*—Blood: total red blood cells 3,480,000; total white cells 7,400; polymorphonuclears 68.0 per cent; lymphocytes 30.0 per cent; large mononuclears 2.0 per cent. Sputum: no tubercle bacilli were detected; a large number of pneumococci and a few streptococci were present. W.R. negative. Pleural fluid protein 5.0 per cent; chloride 725.0 mg. per 100 c.c.m., sugar *nil*, urea 53.5 per cent, calcium 9.0 mg. per 100 c.c.m., positive Rivalta's test, van den Bergh test indirect, faintly positive; total cells 9,728 per c.m.m., polymorphonuclears 7.0 per cent, lymphocytes 74.0 per cent, eosinophils 14.0 per cent, monocytes 5.0 per cent, on microscopic examination no organisms were found but on culture pneumococci were isolated. X-ray of the chest showed pleurisy with effusion on the right side with no visible lesion of either lung.

Guinea-pig inoculation of the fluid was done and revealed no tuberculous infection.

*Progress and treatment.*—A course of M&B 693, 2 tablets every 4 hours, was given for 5 days, but the amount of fluid remained the same after the treatment. The pleural fluid was again sent for culture and pneumococci were isolated, and the cellular count showed total cells 3,200 per c.m.m., polymorphonuclears 30.0 per cent, lymphocytes 56.0 per cent, eosinophils 14.0 per cent. After one week's interval another course of treatment with M&B 693 was given. After another week the fluid was again drawn out. The fluid was sero-fibrinous in character; it showed a cell count of 823 per c.m.m. and pneumococci were isolated by culture. In spite of a month's treatment with M&B 693 there was no reduction in the amount of fluid, and viable pneumococci persisted although cell counts revealed a gradual reduction in number. In the absence of any indication of absorption of the fluid, an aspiration was done and 2 pints of the fluid were drawn out and 200 c.c.m. of air were introduced. After a fortnight the patient was x-rayed again, and a small hydro-pneumothorax was noted on the right side. A small amount of fluid was drawn out and it was sterile after culture. The patient remained afebrile throughout.

After another fortnight no fluid was present in the pleural cavity. He was cured and discharged. The case was followed for two months after his discharge from the hospital and he had no further effusion or any other complaint.

### Discussion

The case closely simulated tuberculous pleurisy with effusion but it was proved to be pneumococcal in origin. The absence of any history of



an attack of pneumonia, coupled with negative clinical and radiological evidences of any pneumonic changes in the lung indicated the diagnosis of primary pneumococcus sero-fibrinous pleurisy, which is undoubtedly a very rare condition. A completely afebrile course was another point of importance. M&B 693 had no effect on the pneumococci as evidenced by the positive culture reports. Aspiration of the fluid combined with pneumothorax proved effective by allowing no further exudation to take place, and no viable pneumococci could be detected in the fluid.

#### Summary

A description of primary pneumococcus sero-fibrinous pleurisy has been given with an illustrative case report.

#### Acknowledgments

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## A NEUROTIC GUILT-COMPLEX UNCOVERED

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#### Introduction and summary

A CASE of a talented pianist is presented showing mixed features of the three sub-groups, anxiety state, conversion hysteria and compulsive-obsessional neurosis, occurring in a schizoid personality. The case appears to be of interest for several reasons. It shows the psycho-pathological mechanisms which led to the production of neurotic symptoms. The patient's intelligence, co-operation, naivety and a remarkable degree of introspection led to the discovery and uncovering of a neurotic guilt-complex. Favourable circumstances made it possible to demonstrate the structure of this complex in a new way with the help of a simple diagram. Emotion, like a smoke screen, rendered the complex invisible to the patient. The cloud of emotion dispersed when he was made aware of its existence. Thus the patient was able to see the connections between his problems and his symptoms. From the moment he understood the causation of all his troubles they ceased to exist. In rare cases like the one described here, a successful result can be obtained in as short a time as 10 days, which includes both analysis and treatment. The method employed was essentially in accordance with those of Freud and Adler.

#### Present complaints

For the last 10 weeks frequent fainting attacks—often 2 or 3 a day. For the last year headaches, inability to concentrate, insomnia, listlessness, anxiety feelings, chest trouble.

#### History

He had a happy childhood, was spoiled and pampered by his parents; he was deeply attached to his mother and admired his father, though he feared him at times. He was a 'cry-baby' and displayed temper tantrums at the age of 4. At school and later at an Engineering College he did well with a minimum effort. Games and sports did not interest him, and he had very few friends. His hobbies were music, reading and painting.

He showed great talent and interest for music at an early age, and had piano lessons for 10 years, after which he passed many musical examinations and obtained the diploma of music as a qualified teacher at an abnormally early age.

At the age of 16 he applied for the job as a pianist with a well-known orchestra but was not accepted on account of his age. In order to remain in the limelight he lowered his standard and played popular music and jazz in popular stage and dance bands in England, and was well paid.

At 20 (1938) he joined the army as a pianist and came to India early in 1939 accompanied by his wife. Though not unhappy he felt that he was gradually drifting away from his childhood ideal of music.

Since October 1942 he had had no opportunity to play the piano and so, to give an outlet to his pent-up feelings, he was sent to an Intelligence Section where he had to do map-drawing, enlarging, logging, etc.

#### Previous and recent illnesses

No serious illnesses in childhood and adolescence. Since joining the army, bronchitis three times. In January and February 1943 severe attack of malaria and jaundice. In March 1943 he resumed work, but could not concentrate, complained of headaches and weakness, and fainted on one occasion for about a minute. At the end of May 1943 he fainted again and woke up in barracks about an hour later. He was confused and disorientated for a whole day. Two days later he fainted twice in the morning, but the 'turns' were short and so was the period of clouded consciousness. From that time onward the fainting attacks came on more regularly, and he had 2 or 3 every day. On questioning him as to whether he ever had fainting attacks before, he stated that he had an isolated one about a year ago. On that day he had felt depressed, off-colour, 'fed up', out of sorts, and he had gone to bed early. Before midnight he felt sick, got up and went to the latrine, vomited, felt better and went back. Just



before reaching the barracks he fainted and woke up the next morning in hospital, where he was kept for 3 days, diagnosed as hysteria.

Another soldier who saw him during a recent collapse describes it as follows: 'He sank to the ground as if his knees gave way. He appeared unconscious for about 15 minutes during which time he trembled all over and breathed peculiarly. His eyes were turned upwards'. There was no description of convulsions, tongue biting and incontinence.

Chiefly because of the increasing frequency of these fainting attacks, the patient was referred to us.

#### *Examination and mental exploration*

The patient, aged 25, of tall and asthenic habitus, shows physically no abnormalities other than myopia and astigmatism. His mental make-up is that of a schizoid personality. He is introverted, narcissistic, egocentric, eccentric, artistic and given to mystical-fantastic day-dreaming. In the foreground are feelings of superiority and unreality. He does not seem to be happy in the world around him. He ponders over the question whether there is life on other planets and what sort of life it would be. He is also much interested in the 'shape of things to come'. He says 'I seem to live in a world of my own' and he gives the following examples:—

Once when walking through a crowd of people it seemed to him as if he was in another world and he got the feeling of being very tall. He looked down on the insignificant crowd as if they were ants which he could easily sweep away.

The noise of the fan suggests to him a particular piece of music coming from a gramophone or radio. When the tune reaches the end but the musical noise of the fan still goes on, he realizes that the music has been an illusion.

When working in the Intelligence Section he noticed that in copying maps he put more into his own drawing than there were in the original map, e.g. temples, rivers, and various other features. He has never been caught making these mistakes but noticed them himself when comparing the maps the next day. He could have sworn that the additional details he put in had been in the original map as well, and was quite surprised to find this extraordinary incongruity.

At times when playing bridge he played wrong cards and realized that his mind had been far away.

Of late, he says, he cannot control his mood. He can laugh and giggle without feeling gay. He knows that it is not a true expression of his feelings.

When walking down a street he can walk by his own side and watch his outer body moving just as if he were looking into a mirror. Streets and houses that he knows seem to him different,

and he wonders whether he has ever seen them before.

He says he has the power of knowing when people talk about him in his absence. He invariably found this to be true and the people who had referred to him always confirmed it afterwards.

As the present holds nothing for him, he lives in the future and builds castles in the air. 'After the war I am going to raise the best band in England. The public is waiting for me. I have a sort of mission to fulfil. My life is designed for it, and the army and the war can't stop me. If you set your mind to a thing, you can do it'.

Opposed to these ideas of omnipotence is a feeling of great uncertainty, an awareness of a conflict in his unconscious mind. 'Some question or problem is hanging over me, but I can't make out what it is. I am puzzled over something without knowing what I am puzzled about. At times I feel I am walking into a dead-end street, unable to get out'.

He often gets dreams of falling and dreams of flying. In the former he falls down a well without ever hitting the bottom (inferiority-complex: a downfall). In the latter he is pulled through space by an unknown force without ever reaching a destination (an ambitious struggle for superiority-leading him nowhere).

A heavy thunderstorm evoked in him the feeling of possessing terrific power. 'I felt like playing the organ in a huge hall. When you play the organ, you get a terrific sense of power. You can bring a whole building down with certain chords. I had the feeling that I was the storm and that I was holding the power. I wanted to play certain chords so loud that it would make the listeners deaf and burst their eardrums'.

#### *Analysis on Adlerian lines,*

His craving for power to the point of destroying people and structures is a good example of Nietzsche's 'will to power', on which Adler based his 'striving for superiority'. Adler's *Individual Psychology* fits our case very well and his methods can well be employed to gain insight into the patient's 'life-line' and to point out to him his futile and inadequate attempts to alter it. At the root of his trouble is the failure in his vocation. The boy grew up with the expectation of becoming famous. His brilliant success in music in the 10 years from 6 to 16 seemed to confirm it. What is he now? A pianist in an infantry-unit and without a piano at that. He received his first major rebuff in life when he was refused the job as pianist in the well-known orchestra on account of his age. It was a shock to his pride, self-esteem, and ambition, and his first clash with reality.

Retreat disguises defeat. The failure in his vocation forced him to beat a retreat. This resulted in the development of a neurosis and

the production of physical and psychical symptoms as described above.

In his struggle to cover up the threatening defeat, he inevitably came into conflict with the world or reality and its social demands. This is evidenced by his feelings of unreality, superiority and aggressiveness, his self-love and lack of interest in others. His unrelenting struggle for superiority is only a mask for his inferiority-complex. His unreality feelings are only an escape, because he finds reality intolerable.

He lives indeed in a 'world of his own', in which some of the laws of the real world no longer exist. However, it is the realization of his own fantastic way of thinking which distinguishes the neurotic from the psychotic. His return to reality is immediate, and there is no true dissociation of the personality.

As a child he envied his younger brother's strong physique, and took tonics, vitamins and milk to strengthen his body. All his attempts failed, and thus the nucleus for the formation of an inferiority-complex was formed. Later it took the form of what Adler calls 'the masculine protest', an overdetermined desire to be a man and an inferiority feeling due to lack of masculinity.

He was always aware of his sexual shyness. Later, when in company with other men who talked and boasted of their experiences with women, he often wished to know more about the subject himself. He detested but at the same time envied the he-man type with his many stories to tell about women. This constitutes the origin of his compensatory craving for power in the non-sexual field.

#### *Analysis on Freudian lines*

*Sex development.*—At 14 his father gave him a lecture, warning him of the danger of sexual intercourse, venereal disease and masturbation, with the result that the patient said to himself 'no women for me'. The idea of a union between a man and a woman disgusted him, and the idea of masturbation seared him so much that he has done it only once in his life. At 18 he became friendly with a girl whom he afterwards married. The first kiss upset him so much that he ran away from her, chased by feelings of shame, sin and guilt. He did not show his face to her for a whole week, though before he used to see her daily. Married, he felt a brute after his first sexual intercourse with his wife, and did not dare to look her in the eyes.

Women in general do not attract him. Dancing does not appeal to him, because it means bodily contact with a woman. He says he has seen too much nakedness backstage. He lives a married life in which sex plays a minor part only. He denies all homosexual tendencies and looks upon them with disgust.

He dislikes cats because they remind him of women, 'who are sly and cunning, deceitful and untrustworthy, who slink and sneak, are full of

spite, malice and bad intentions. Even in their affections they are not genuine and you can be sure that they want something from you. One can read their mind in their eyes as one can in the horrible yellow eyes of a cat. Why can't I enjoy their company? Why don't I allow myself to be deceived by them? Because I know them and can see through them. Their eyes betray them as they betray the cat. Women and cats are identical'.

His favourite colours are blue and green. They are soothing and denote softness. He does not care much for red and white. Red is harsh and white is solid and hard. Black he associates with death and funerals. Yellow and grey he strongly detests as they remind him of something 'dirty, evil and sinful'.

Here we get a link between women—cats—yellow eyes—sin—women. He now recalls two further incidents which strengthen this simple chain of associations.

'At 15 I was impressed by the remarkable power one of my schoolmates possessed of forcing his will on people by staring at them. He got a younger boy under his influence and dominated and bullied him. I wondered if the bigger chap could have managed to get a grip on me, but I think I would have stared him out. His eyes were like cats' eyes'.

In 1940 he read *Mother India* and in it a description of a man who died because another person had cast an evil eye on him.

His belief in the power of hypnosis, which forms an additional link, gives us further insight into the causation of his symptoms, particularly of the fainting attacks. He describes them as always being preceded by a vivid visual sensation. He sees his own eyes looking at him; the eyes go round and round; he feels hypnotized; has to close his eyes; is unable to re-open them; everything turns black and he faints. The eyes staring at him are yellow with wide black pupils. They appear on a bright red background, the periphery of which is dark (see figure 1, plate XV). He wakes up with a headache lasting for hours, unrelieved by aspirin, of which on one occasion he took 12 tablets. He is in a daze for 5 minutes, when the curtain slowly lifts and he feels well again.

Every night before falling asleep he gets a terrible oppressive sensation in the chest. He sees a tiny black circle against a yellow background (see figure 2, plate XV). The circle grows bigger and bigger and comes nearer and nearer, till it eventually encircles him. He feels overpowered and covered up, choked and suffocated, has to get up and walk about, smokes a cigarette, goes to bed again and reads himself to sleep. During this horrible possession he is terror-stricken, he perspires and breathes heavily and fears that one day he may not be able to get up in time.

After eight sessions I asked the patient to make a drawing of his recurring nightly oppressions and of the visual sensation which

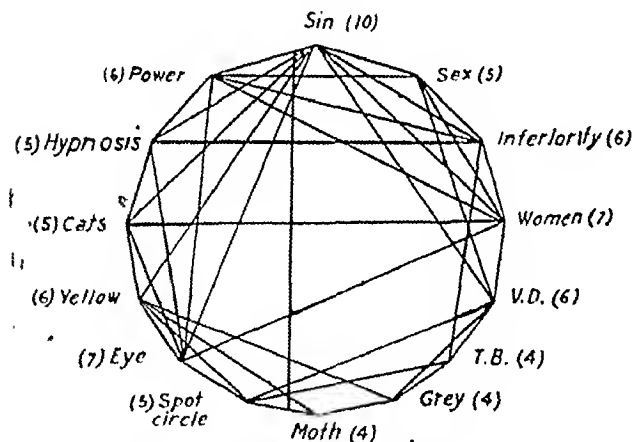
preceded the fainting attacks. The drawings are reproduced here. Putting them on paper enabled the patient to look at his own artistic production in an emotionally detached way. He felt a relief as if he had got rid of his obsessions altogether. In tracing back the origin and onset of his attacks the patient recalls an incident which happened about a year ago. This coincides approximately with his first faint.

A clarinet player in his band showed signs of being 'short-winded' and collapsed on several occasions. He was taken to hospital and tuberculosis was diagnosed. Our patient wondered whether he too might suffer from tuberculosis as his way of breathing was very similar.

This marked the onset of his sighing respiration. Before relating this incident he had complained to me of oppressed breathing and of feeling 'very thick on the chest' and of bringing up 'bad tasting, smelly phlegm'. It worried him and he asked 'people suffering from consumption are short-winded, aren't they?' He had two sputum tests a few months ago, both negative.

Fig. 3.

Internal structure of complex.



The figures in brackets denote the number of obvious inter-associations.

His conception of tuberculosis is that 'part of the lungs is eaten away and replaced by smelly rotten flesh'. That is why he feels 'thick on the chest' and brings up 'bad tasting, smelly phlegm'. He immediately associates consumption with venereal sores. Both consist of rotten flesh and are grey in colour. Both grow bigger and bigger till they consume the whole body (see nightmare figure 3). Both must look the same.

To sum up in a few words the material gained so far, we may assume that the nightmare as well as the fainting attacks are produced by a hypnotic power the symbol of which is the eye. He apparently wishes to possess the power of hypnotizing but refrains from exercising this power on others. He hypnotizes himself rather than be overpowered by others or by sin (? masturbatory equivalent). He fears to fall a victim

to sin as embodied by women. He distrusts women and identifies them with cats.

His fear of tuberculosis stands for fear of venereal disease. Previously, after his father's lecture, he had linked up sex-sin-venereal disease-women. Now tuberculosis, grey and yellow eyes, and cats are taken additionally into the complex.

During the fourth interview a moth fluttered about the room. The patient followed it with his eyes nervously, appeared highly excited and completely distracted. The moment the moth settled down on the table he got up and killed it with a match-box and crushed it to dust. He had a terrific emotional reaction, tears welled into his eyes, he blushed, trembled, broke a pencil into two, nervously took a cigarette and was hardly able to light it. After calming down he said 'I hate them. There is something bad and evil about them all. I have to get rid of them and kill and crush them. Unless I destroy their shape, I won't feel relieved'.

At times, he says, his skin feels as though being touched by a moth and his horrible feeling makes him shudder and evokes in him a sensation similar to the one experienced when seeing a moth.

After much pressing he recollects two incidents which he had not recalled since their happening.

At the age of 7, he glanced through Cassell's *Book of Knowledge*, and his eyes fell on an illustrated page depicting various kinds of moths. Some were grey and some were yellow and some had dots and circles on their wings. He felt an immediate dislike for them, which persisted.

At 10 he was deeply impressed by a book on life after death, in which it was stated that the soul leaves the dead body and assumes another shape. He then linked up that the soul of evil-doing people and sinners must assume the shape of a moth. This established the association between moth and sin.

A dream further illustrates this new connection. A few days ago a heavy storm and lightning made him dream of being in action. There was an attack by dive-bombers and he ran as fast as he could, chased by a low-flying bomber which then changed into a moth, and suddenly he saw thousands of them. He woke up and jumped out of bed.

This dream reminds one of the intense feeling of guilt, shame and sin, by which he was 'chased' after his first erotic adventures.

### Conclusion

The internal structure of his complex, as I see it, is given in the diagram. It could be demonstrated still better, if located in a sphere instead of a circle. Associations of ideas are not links of a chain, but more like a polygonal body with its sides and angles copiously inter-linked.

A complex of diverse ideas, welded together by a powerful childhood emotion, was laid

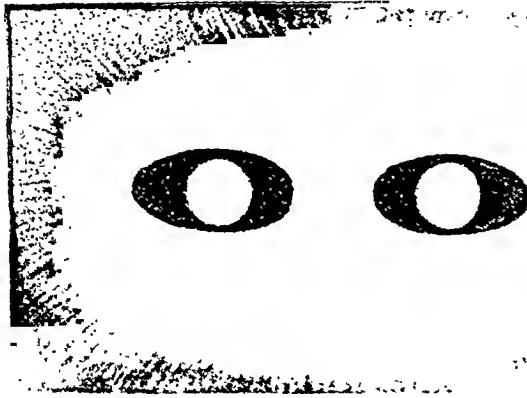


Fig. 1.—Patient's fainting of visual sensation before the fainting attack. Background red, eyes yellow.

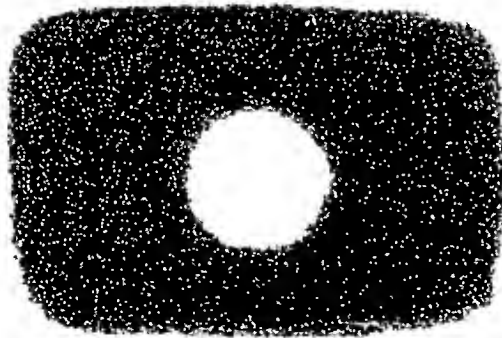


Fig. 2.—Patient's fainting of visual sensation before asleep. Black circle against a yellow background.

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\* Redrawn from the original colour paintings provided by the author.—*Editor.*

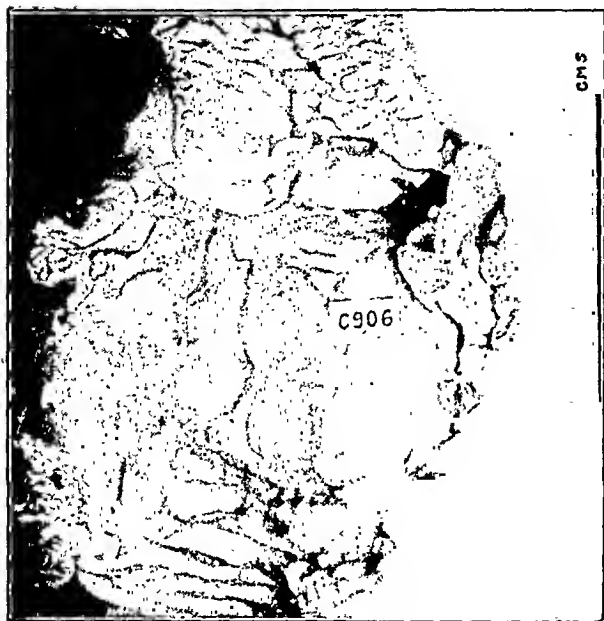


Fig. 1.—Gross specimen.



Fig. 2.—Histological appearance : magnification  $\times 90$ .

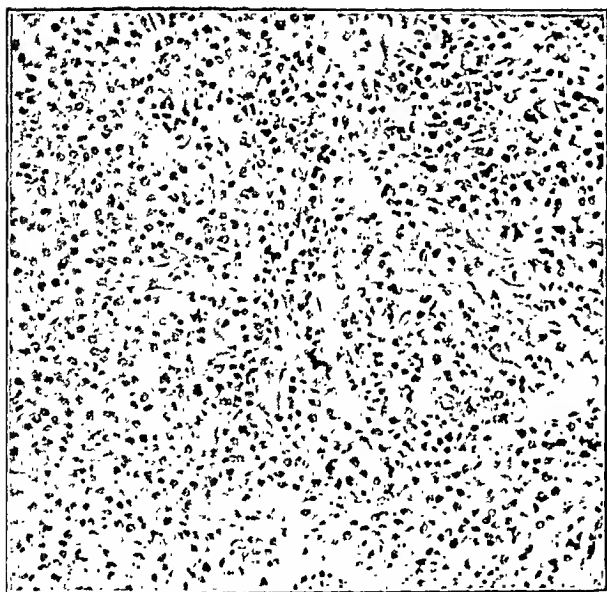


Fig. 3.—Histological appearance : magnification  $\times 180$ .

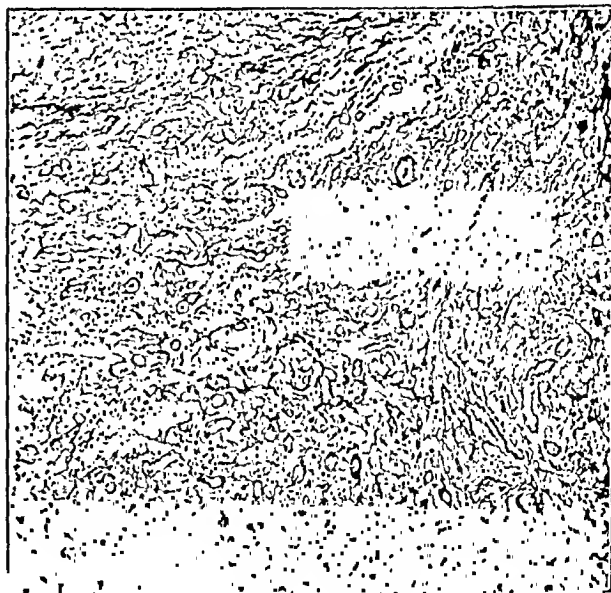


Fig. 4.—By silver impregnation : magnification  $\times 90$ .

bare. I strictly adhered to the analytical principle to play as passive a rôle as possible. No suggestion treatment, hypnosis or re-education was attempted.

The subject lent itself well for a division—though artificial—into Freudian and Adlerian ways of viewing a case. An attempt has been made to sift the analytical material and to make it more easily comprehensible to the reader. I feel that in omitting either view-point the case would have been of less interest and would have required a longer time to respond to treatment.

The patient had no further fainting attacks, no terror dreams or anxiety feelings, and has refrained from killing moths ever since. The inability to concentrate, listlessness, headaches, sighing respiration and other chest symptoms have disappeared and the therapeutic result has been maintained up to date, 5 months since the analysis.

My thanks are due to Colonel M. Taylor, I.M.S., Medical Superintendent of the European Mental Hospital, Ranchi, for his encouragement and for his permission to publish the case.

## A Mirror of Hospital Practice

### A CASE OF LYMPHOSARCOMA OF THE ILEUM

By D. A. ANDERSEN, M.B., F.R.C.S. (Eng.)

Chief Medical Officer, The Salvation Army Evangeline Booth Hospital, Ahmednagar

**History.**—The patient was a shoemaker, aged about 35. He attended the out-patients' department complaining that he had suffered from pain in the left iliac fossa for about 6 months and noticed a lump there for 4 months, which had gradually increased in size. There had been no distension or vomiting, and the bowels were open regularly. He had no cough or fever but had lost weight recently. Nothing significant was elicited in his previous history, either personal or family.

**Physical examination.**—30th January, 1943. Temperature 98°F.; pulse 90; respiration 22. General condition: He was thin but did not look ill. On abdominal examination, there was a mass in the left iliac fossa, deep to the parietal muscles, about 3½ inches in diameter, roughly spherical in shape, with an irregular surface and moderately firm in consistency. It moved freely for 2 to 3 inches in any direction, as if attached by a pedicle to the posterior wall of the fossa, and could not be pushed into the pelvis. The liver and spleen were not felt enlarged. No other masses felt. No free fluid.

P.R.: Nil.

Chest: Clinical examination and screening negative.

Urine: Normal.

Blood count: R.B.C. 4½ million; Hb 92 per cent; W.B.C. 7,400; polymorphonuclears 70 per cent; lymphocytes 28 per cent; eosinophiles 2 per cent. No malaria parasites.

Stool: No ova; no amœbæ or cysts; no gross blood or mucus; a few leucocytes and R.B.C.s. O.T. 1:1,000 negative.

The diagnosis was uncertain and laparotomy was decided upon.

**Operation.**—5th February, 1943. Anaesthetic, ether chloroform mixture (7:3).

**Incision:** Left lower paramedian.

**Findings:** The mass presented at once and was found obscured by omental adhesions. When these were cut it became obvious that the mass was (a) a swelling of the presenting ileum and (b) a lymphatic mass in the adjoining mesentery which arose directly from (a). No other glands were seen to be involved, and the rest of the ileum appeared normal. There was no distension of the bowel above the tumour.

**Procedure.**—A resection of the tumour including about 4 inches of healthy gut on each side was performed, and the leaf of mesentery removed with it just included the enlarged lymphatic mass with a narrow margin. The mesentery was taken up by the tumour and was very short, making it difficult to remove a larger margin. The ends of the bowel were closed by Mikulyicz' method with no. 1 chromic intestinal gut, and a side to side anastomosis performed 1½ inches above the closed ends. Sulphanilamide powder was applied to the suture lines.

**Post-operative progress.**—The temperature did not rise above 99 till the 4th day when he developed bronchitis, and on the 6th day there was a temperature of 102, which was however controlled in the next 24 hours by the administration of M&B 693 grammes 3 daily after which he remained afebrile. The abdomen throughout was soft and not distended, and there was no vomiting, and flatus was passed in 24 hours. Fluids were given parenterally for the 24 hours, after which they were given gradually by mouth, supplemented by rectal drip for as long as necessary. Soluble sulphanilamide, 10 c.cm. 10 per cent, was given six-hourly for the first 24 hours as a prophylactic measure. Sputum examination on the 6th day after operation was negative for T.B. Further convalescence was uneventful, and he was discharged after 24 days in hospital. He was advised to attend the Tata Memorial Hospital for deep x-ray treatment but failed to do so.

**Pathology.**—Gross examination (see figure 1, plate XVI). A specimen of excision of the ileum measures 23 cm. in length. The wall of the intestine is thickened by a white tumour mass completely encircling the bowel for about 7 cm. in length. On opening the intestine the tumour is found to have ulcerated over the major portion of its inner surface. The change from the tumour to the healthy bowel wall is abrupt. The thickness of the wall of the bowel in this region is 3½ cm. The tumour is seen infiltrating all coats of the bowel wall and extending into the mesenteric nodes. There is a normal piece of the mesentery beyond the tumour mass.

**Microscopical examination.**—The histological examination shows a homogeneous infiltration of all the coats of the bowel by small round cells (see figures 2 and 3, plate XVI). The cytoplasm of these cells is faintly basophilic and forms a narrow rim around the nuclei. The nuclei have a thick nuclear membrane and contain coarse masses of chromatin. The neoplastic tissue is continuous with the tumour mass outside the wall of the intestine. By silver impregnation (Gomori) the reticulum is seen passing round tumour cells in a basket-like fashion (see figure 4, plate XVI).

**Diagnosis.**—Lymphosarcoma.

**Follow-up.**—The patient remained symptom-free for 5 months, but then developed an obvious recurrence in the original site about 2 by 1 inches in diameter. He then consented to attend the Tata Memorial Hospital but unfortunately absconded soon after admission. He did not present himself again to me for treatment, but attended a local practitioner. I am reliably informed by a fellow shoemaker from his vicinity that he died in December 1943, about 17 months after noticing the first symptoms, and 11 months after the operation.

**Comment.**—The differential diagnosis lay between a tuberculoma of the lower ileum similar to the more common tuberculous caecum, or a lymphosarcoma. Against tuberculosis was the absence of evidence of tuberculosis elsewhere.



and a negative tuberculin test but the diagnosis finally rests on the microscopic findings for which I am indebted to Dr. Khanolkar. The other question that arises is whether the glandular focus in the mesentery is primary or secondary to the intestinal lesion. To quote from Boyd's *General Pathology*, 'In some cases the intestinal involvement is so great, converting the bowel into a stiff tube, that there is no room for doubt regarding the starting point of the condition'. The present case reported appears to fall into this group.

As unfortunately frequently occurs, the patient failed to carry out the advice given. It is just possible that, had the patient received a full post-operative course of deep x-rays to the operation area and the regional glands, a recurrence might have been prevented.

The pathological investigation and the preparation of the photographs of the gross specimen and the histological appearances were kindly carried out by Dr. V. R. Khanolkar, Director of Laboratories, Tata Memorial Hospital, to whom I tender my thanks.

#### REFERENCE

- Boyd, W. (1943) .. *A Textbook of Pathology*.  
Lee and Febiger, Philadelphia.

### INFARCTION FOLLOWING THE USE OF AN ABORTIFACIENT

By P. L. DESHMUKH, M.D., D.T.M. & H., F.C.P.S.  
Poona City

A MARRIED LADY, aged 25, was 3 months' pregnant. She had five living children and was advised abortion because it was thought that frequently repeated pregnancies were likely to endanger her health. Her doctor undertook to do the operation by using one of the abortifacient pastes (Aeratus), which he believed to be safe. After the preparation of the patient, the paste was injected very slowly between the membranes and the uterine wall. There was slight bleeding and suddenly the patient had a severe fit of cough and became cyanosed. She complained of severe pain in the chest and the loins. The next moment she was unconscious, pulseless and perspiring profusely. Coramine 4 c.cm. and adrenaline  $\frac{1}{2}$  c.cm. were given subcutaneously, and artificial respiration was started. Gradually the patient came round, and when I saw her, within 20 minutes of the collapse, she was conscious and able to recognize and talk. She still complained of severe pain in the left side of her chest and in the left loin. After a while she had a bout of coughing and the sputum was blood-tinged. About the same time she passed scanty urine with a fair amount of blood in it. One hour later, pleural friction and crepitations could be heard in a localized area in the left axillary region. Her cyanosis gradually disappeared after oxygen inhalations, but the pulse remained weak and rapid. The urine contained obvious blood for the next 48 hours, and gradually it cleared up. After 12 hours abortion occurred. She was then treated as a case of pneumonia with M&B 693 tablets and occasional stimulants. The patient made an uneventful recovery.

**Discussion.**—The symptoms appear to be due to the occurrence of pulmonary and renal infarction. Cerebral embolism was suggested by the unconsciousness that supervened, but it could be excluded by the absence of evidence of

cerebral damage such as paresis or paralysis on returning to consciousness. The severe and sudden pain in the chest with signs of collapse suggested embolism of the coronary artery; but the absence of pallor, vomiting and, later, signs of pericarditis were against such a diagnosis. Cyanosis, blood-tinged sputum, pleural friction and crepitations indicated pulmonary infarction. The acute pain in the left loin with hæmaturia can only be explained by assuming infarction of the left kidney. Another explanation which is less satisfactory is that the renal symptoms are caused by acute nephritis produced by chemical irritant introduced in the blood with the paste. The points against such an assumption are the suddenness of symptoms, the absence of cedema, the absence of casts in the urinary deposit and the rapid clearing of the urine that followed. It is doubtful whether the minute amount of the irritant injected with the paste can produce a fulminant irritation of the kidney such as to give rise to marked hæmaturia. The loin pain was unilateral while an irritant carried in circulation would give rise to bilateral symptoms. Thus, renal infarction appears to be a more feasible explanation of the clinical picture. It is difficult to account for the embolism in the systemic circuit after aspiration of the foreign material by the uterine veins, except as a paradoxical embolism. The heart did not show any evidence of valvular disease or of a congenital anomaly that is likely to give rise to paradoxical embolism. In the latter condition it is usually the cerebral vessels that are affected. Here it has given rise to renal infarction.

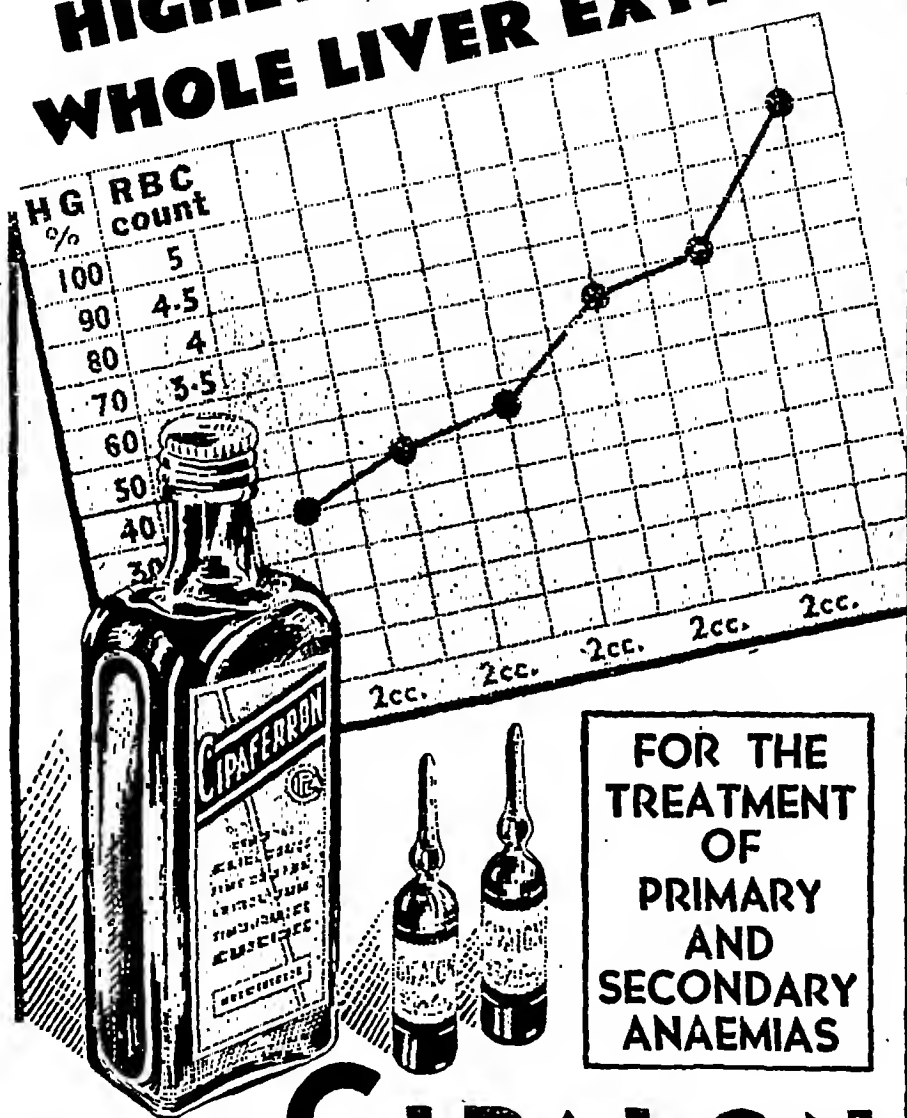
The symptoms obviously appeared after the accidental injection of the paste in the vascular channels. The disaster that followed could, perhaps, have been avoided if the injection had been stopped as soon as the bleeding was noticed.

The interest of the case lies in the following points:—

1. Dangerous complication such as pulmonary and renal infarction appeared during a comparatively trivial operation.
2. Embolism appeared simultaneously in the pulmonary and the systemic circulation.
3. The systemic embolism, if it has occurred, has evaded the cerebral vessels and occurred in the renal vessels, which is unusual. The mechanism of the embolism has remained unexplained.
4. The administration of M&B 693 in the presence of a renal infarction produced no apparent harm.
5. The pulmonary infarction responded well to chemotherapy.
6. The injection of the paste after the occurrence of the bleeding appeared to produce the dangerous symptoms seen in this patient.

[Note.—There is no apparent reason for the administration of sulphapyridine in this case.—EDITOR, I. M. G.]

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# Indian Medical Gazette

JULY

## SMALLPOX IN CALCUTTA

Of the diseases that are notifiable in Calcutta, smallpox is one of the most important. It is more easily prevented than any other disease of this group, yet in no year has the city remained free from it, and its average rate of mortality during the decade 1930-39 was higher than in any other part of Bengal. Epidemics are common, and these happen so frequently and regularly that smallpox has come to be regarded as part of our destiny.

For some months past Calcutta has been in the grip of an epidemic which threatens to be a record one, considering its duration and severity. Its most remarkable feature is the high death rate which, according to the figures available to us, was a little over 80 per cent during the first four months of this year. This figure is probably more apparent than real. The most likely explanation is that many persons neglect to notify the occurrence of the disease as they should. Consequently, the health authorities receive more accurate information about the number of deaths from smallpox than that of actual cases.

It would be interesting to know the vaccinal condition of the persons who developed the infection, but we are not in a position to throw light on this point. Certain available figures are however highly suggestive. Thus during the first three months of the year, 14 per cent of the deaths occurred in infants under 1 year of age, 39 per cent in children from 1 to 5 years and 33 per cent in people of 10 years and above. These indicate that primary vaccination is in many instances not done at the right time, thus leaving a large number of children exposed to the infection of a disease which is always amongst us, and that re-vaccination is not done on a sufficiently large scale to add to the immunity which tends to pass off in a few years after primary vaccination. There are no reasons for believing that conditions were any better prior to the influx of large number of people that has taken place in Calcutta during the last two years and that has undoubtedly added to the difficulties of the Corporation. Vaccination is the only thing known to give protection against smallpox, and while unprotected individuals are of course a danger, it is the presence of a large susceptible population that spreads the disease, and this is at the background of Calcutta's problem. It should be our aim to reduce, or better abolish, this susceptible population. It is not enough to vaccinate vigorously during an epidemic; it does not require much persuasion at this time, for fear acts as a stimulus. It is

with the passing away of the epidemic when vigilance tends to relax that the number of susceptible persons increases, creating conditions favourable for fresh out-breaks.

The remedy is obvious, and that is to enforce the vaccination laws and introduce compulsory re-vaccination, the need of which is also evident from the Health Officer's Annual Report for 1942-43. In this year, 4,560 infants under 1 year were not vaccinated. No wonder that 'infants and children under 1 year and of 1 to 5 years of age suffered more severely than others', although smallpox occurred only sporadically during most of the year. He refers to the poor response to vaccination and says that 'many persons, especially the *bustee* people, go unprotected and refuse re-vaccination'. A scheme for compulsory re-vaccination is, however, pending before the Corporation. As regards notification, he remarks 'the response of the public and the medical practitioners in this direction is very unsatisfactory. Although there is penal law for its enforcement, many practical difficulties arise if legal action be taken'. This is a frank statement, but offers no solution to the problem.

Health propaganda work is carried out in the city, but we would like to see more intensive work of this nature. During the height of the present epidemic it was not unusual to see smallpox patients, convalescent but still in the infective stage, walking about in the crowded streets; nobody seemed to mind their presence. Such thoughtless actions undoubtedly spread the disease.

Lastly, there is an urgent need for a modern hospital for infectious diseases in Calcutta, preferably in open-air surroundings, which should be well-equipped so as to attract both rich and poor patients. According to the Health Officer's figures, only 120 beds are available for smallpox patients. This accommodation is obviously very inadequate, and the matter requires serious attention.

R. N. C.

## WHEAT AND THE WAR

### HOW TO MAKE SHORT SUPPLIES OF WHEAT GO FURTHER

SUPPLIES of food, and of wheat in particular, constitute a dominant factor in the prosecution of war. In the last world war, the slogan, 'Wheat will win the war', was widely voiced in the United States, and Starling in Britain observed that 'any shortage of bread must cause widespread hardship as well as industrial inefficiency and unrest'. Similar sentiments prevail in India to-day in the midst of the present world war. Owing to the cessation of supplies from Burma, India is now short of two million tons of rice, and this shortage has increased pressure on available supplies

of wheat. Further, various causes such as increased military needs, hoarding, speculation, etc., have added to this pressure. In spite of a record crop in 1942, and of importation from other countries, the demand for wheat is so great that any measure which is likely to give relief must be welcome. With this object certain experiments were carried out in the Punjab to find out whether cheaper grains such as *jowar* and *bajra* of which there is no scarcity could be mixed with wheat—both for making loaves of leavened bread (*dabal roti*) and unleavened pancakes (*chapattis*) without noticeably altering their appearance and quality. The result of the investigation is contained in a small pamphlet, 'Optimum proportions of grains capable of admixture with wheat', by Messrs. Ram Dhan Singh, S. Rattan Singh and Mohammad Rafiq, of the Punjab Agricultural College, Lyallpur (reprint from *Indian Farming*, July 1943).

The grains experimented with were barley, *bajra* (*Pennisetum typhoideum*), *jowar* (*Andropogon sorghum*), maize and rice, and three varieties of pulses, viz, gram, *mash* (*Phaseolus mungo*) and *mung* (*Phaseolus aureus*). These grains are by themselves incapable of making a loaf owing to the absence in them of the proteins, known as gluten, which are present in wheat. The optimum proportions in which these grains can be mixed with wheat without affecting the quality and acceptability of the resulting loaf and *chapatti* have been found to be as follows. (per cent):—

Grain	For loaf	For chapattis
Barley .. ..	10 to 15	15 to 25
<i>Bajra</i> .. ..	10	15
<i>Jowar</i> .. ..	7 to 10	15
Maize (white) ..	10	25
Maize (yellow) ..	7	20
Rice .. ..	5	Not determined.
Gram .. ..	5 to 7	Do.
<i>Mash</i> .. ..	5	Do.
<i>Mung</i> .. ..	5	Do.

It is well known that the pulses are commonly mixed with wheat for making *chapattis*, *puris*, *kachauris* and *paraothas* more tasty and nutritious. Their use, however, in making loaves is probably not an economic proposition, costing, as they do, more than wheat, nor does it appear from the pamphlet that they contribute to the making of good loaves, although gram does improve their taste. Rice also is not satisfactory. But with mixtures of wheat and other grains, loaves and *chapattis* can be prepared, which are not at all inferior to pure wheat preparations in appearance and taste. They however tend to reduce the loaf volume, but *bajra* increases it. *Bajra* mixture also adds to the taste and flavour of *chapattis* and probably makes them richer in certain nutritive elements such as fat, mineral matter, iron and carotene, but it should be rapidly baked after kneading,

otherwise the dough becomes so lax and loose that it becomes difficult to handle.

Among well-to-do people there is a prejudice against the use of these grains in their daily bread, probably because it does not give the colour of the pure white preparation. But used in the above proportions they yield quite acceptable loaves and *chapattis*, and if they do not put undue strain on the digestive system then the prejudice ought to go, and this would help in making the available wheat go a long way. India produces barley, *bajra*, *jowar*, and maize to the extent of 12 to 13 million tons.

It is obvious, however, that these findings can be properly applied only by issuing ready-made the recommended mixtures from the manufacturing sources themselves, instead of leaving it to the option and convenience of the public, so it remains to be seen what the manufacturers have got to say in the matter, for as the authors of the pamphlet point out, the preparation of flour from the grains on a commercial scale may require further research and modification of technique on the part of the millers.

R. N. C.

### TUBERCULOSIS IN INDIA

THE editor has recently received a copy of the fifth annual report of the Tuberculosis Association of India which has been working steadily in spite of war-time difficulties. It may be recalled that the Marchioness of Linlithgow laid down the office of President of the Association on the 20th October, 1943. Before coming out to India in the year 1936 she was intimately connected with the tuberculosis movement in England where she was the Vice-Chairman of the Papworth Village Settlement. Soon after her arrival, she inaugurated an appeal to raise funds for an anti-tuberculosis campaign in India. A sum of Rs. 85,07,888 was collected and the Tuberculosis Association of India was formed in February 1939 with branches in all the provinces and many Indian States. During her presidentship the total number of tuberculosis sanatoria and hospitals grew from 47 with a bed accommodation of 2,255 in 1936 to 65 with a bed accommodation of 4,328 in 1943, and during the same period the number of clinics increased from 42 to 113; and facilities are now available for training of tuberculosis workers in well-equipped and staffed institutions. Lady Linlithgow will always be remembered in India with gratitude for her initiative and stimulating interest in anti-tuberculosis work, and it is unfortunate that the rapid progress of the movement should have been impeded by war conditions. Her Excellency the Viscountess Wavell is now the President of the Association which can confidently look forward to further solid progress.

Lieutenant-General Sir Gordon Jolly retired from the Chairmanship of the Association during

the year after having ably held the office for just over four years, and has been succeeded by Major-General J. B. Hance. It is gratifying that Sir Gordon Jolly has agreed to serve on the Central Committee as a co-opted member.

It is sad to have to record the death of Dr. C. Frimodt Möller, a foundation member and the first Medical Commissioner of the

Association. He was connected with India for 36 years. As Lady Linlithgow said in her farewell speech, 'he combined vast knowledge, great powers of organization, strength of character and charm of manner which will be almost impossible to replace'.

R. N. C.

## Special Article

### WOUNDS OF THE EXTREMITIES\*

By C. J. HASSETT, M.B.E.

MAJOR, I.M.S.

*Agency Surgeon, North Waziristan, Miranshah*

THE treatment of wounds has undergone a radical change since the last war. During that period, the rival merits of antiseptics in the control of wound infection were adumbrated to the exclusion of the simpler and original principles of Lister who sought to keep infection from wounds and insisted on the reparative defence powers of the body. This is quite different from endeavouring to destroy infection with antiseptics which result in an assault on the reparative powers of the body and violate the principle of rest. The methods of to-day show no difference from the methods of Lister, though the technique in their application may differ. The mortality in gunshot wounds of the femur in the last war was in the region of 80 per cent, differing little from that which occurred in the Crimea. At the end of the war it was in the region of 20 per cent. Trueta (1939) in the recent Spanish war had a mortality of one case in a series of 101 cases.

*The wounds.*—Bullets, fragments of shell or bombs travel in the limb in the line of flight of the missile, and the wound track depends on the position of the limb at the time of wounding. This fact must be borne in mind.

The wound of entry of bullet wounds is generally smaller than that of exit, but in uncomplicated through-and-through flesh wounds their entrance and exit wounds approximate each other in size. I have seen a case in which a bullet pierced both thighs behind and it was difficult to tell in either thigh which was the wound of entry or exit.

Where a bone is involved, the wound of exit, if present, may be many times larger than the wound of entry, because of the disruption of the bone or of the turning of the bullet in its long axis.

In the ragged wounds produced by a bomb or shell splinter, it is easier to decide the site of entry. The destruction of tissue, vessels, nerves

and bones will be so severe that there may be complete ablation of the limb. In the case of bullet wounds involving bone (this I have found common in Waziristan) there may be no exit wound, and the bullet or disintegrated parts of it will be found in the bones and beyond, buried in the soft tissues. The violent disruption of the bone or bones may lead to a large gap, and fragments of the bone are pulverized and displaced a considerable distance into the surrounding muscles (see figures 1, 1a, 1b and 1c, plate XVII).

Through-and-through bullet wounds of the soft tissues are relatively clean, and may be left, but this requires careful judgment as will be subsequently described.

*Injuries to arteries and nerves.*—Along the course of the missile, for a variable distance depending on its size and velocity, there is an area of necrosis. In this area, blood vessels and nerves may be damaged, the former giving rise to hæmorrhage which may be fatal; damage to the latter will produce the signs characteristic of the various nerve lesions. An incomplete wound in an artery bleeds continuously, causing death if not dealt with; whereas a completely severed artery will bleed profusely for a few moments and then cease, as the elasticity of the arterial wall gradually withdraws the wall from the site of injury and envelops the severed end in a mass of adventitia. In animals (rabbits), I have found that bleeding ceases within three minutes where complete division of an artery is carried out. In incomplete division, death occurs after four minutes without cessation of bleeding. In a divided posterior tibial artery I have seen hæmorrhage cease due to this retraction. Lieut.-Colonel L. K. Ledger, I.M.S., also described to me a case which he dealt with where the femoral artery was completely divided and a similar condition had occurred. The artery was subsequently dealt with successfully.

An artery may suffer from concussion without demonstrable injury, producing local spasm which may disappear. Another type of injury is a localized contusion causing rupture of the intima distally or by the liberation of an embolus, may cause gangrene. Another sequel may be necrosis

\* Read before the British Medical Association, Peshawar Branch, on 15th December, 1942.



of the contused wall and secondary hæmorrhage either externally through the wound, producing death from hæmorrhage, or into the tissues around the lesion producing a pulsating hæmatoma leading to the formation of a sacculated aneurysm. Should artery and vein be both involved in the process, a varicose aneurysm may occur.

*Infection of wounds.*—Whether large blood vessels are damaged or not, blood pours out into the track from the damaged muscle and bone, and pieces of missile, clothing, earth, stone or other foreign bodies may be found; moreover, the area is contaminated with organisms from the skin or area where the wounding has occurred.

For a variable period of time after the receipt of the wound, the limb is numb due to the concussion; as a result the individual suffers from wound shock and hæmorrhage which may be severe. In such a devitalized anoxæmic area full of blood clot and serum, favourable conditions are present for the growth and dissemination of both anaerobic organisms and aerobic organisms, as these latter may be facultatively anaerobic.

Such wounds are regarded as being contaminated up to a period of six hours, and may be dealt with so as to bring about healing by first intention in very favourable conditions. After this period, wounds are to be regarded as being infected; the organisms have established themselves. The virulence with which they do this varies with the amount of trauma which the limb has suffered, the interference with the blood supply, and the soil and climatic conditions where the individual was wounded; in some cases, the injudicious use of a tourniquet will favour infection.

In injuries seen after the first 12 hours, the patient will have fever and a raised pulse rate. He will complain of pain in the affected limb. The affected part will be red, brawny and œdematous, with a sero-sanguineous or frankly purulent discharge. The whole limb may be involved, as the organisms tend to spread rapidly along the relatively avascular fascial spaces. If hæmolytic streptococci are present, a rapidly spreading cellulitis or lymphangitis may occur. The neighbouring groups of lymphatic glands are enlarged, swollen, and tender, and localized abscesses may develop. In severe cases, septicæmia may result. If the bones are involved, there is a concomitant osteomyelitis.

If anaerobic gas-producing organisms have established themselves in such traumatized limbs, the onset of gas gangrene is often fulminating, and may declare itself within a few hours of the injury. In less fulminating cases the infection may not declare itself for 24 to 48 hours, and this commonly occurs where surgical aid is delayed or is ineffective.

Clinically, gas gangrene declares itself by the onset of violent pain in the wound, an increase in the volume of the limb, a sudden rise of pulse rate in relation to the temperature, sunken eyes

and a general appearance of grave illness. There is an icteric tinge, and intense thirst. In the affected limb, there is œdema, a brownish discoloration around the wound, and a brownish frothy sero-sanguineous discharge, and a mousy odour which is characteristic. Palpation of the limb reveals crepitation, and on flicking it with the finger a drum-like note is obtained. The presence of emphysema in a wound may excite suspicion of an incipient gas gangrene, but the absence of the other clinical signs should obviate this. In delayed cases, no one can make a mistake.

### *Treatment*

(a) *Preliminary.*—As a general rule, all injuries of the lower limb should be placed in a Thomas splint as soon as possible, and those of the upper limb by padded splints and binding to the trunk for transportation.

I have not encouraged the systematic use of the tourniquet because of its misuse in the hands of the inexperienced; damage may be caused which is worse than the original injury. It should only be used if the limb is completely shot away or if the hæmorrhage comes obviously from a main artery. The routine use of a tourniquet causes pain and shock, and predisposes to gas gangrene by causing anoxæmia of the tissues. A firm pad and bandage will in most instances control hæmorrhage. In four years in my area we have never had occasion to use a tourniquet except in the operation theatre.

Three thousand units of anti-tetanic serum and anti-gas gangrene polyvalent serum are given, and if it is likely that the situation will not allow of evacuation within the first 12 hours, a full course of sulphathiazole is given. Free fluids are given unless the injury is complicated by an abdominal injury. Morphia up to  $\frac{1}{2}$  grain is given. The problems of evacuation to a suitable surgical base will vary with the situation. These will differ in, say, a city subjected to enemy action compared to the battle front; whatever these problems are, it should be our object to give adequate surgical care to wounded within the first six to eight hours. That is an ideal which may not always be practicable.

(b) *The fracture.*—Prior to any operation on a compound gunshot fracture of the limbs, immobilize the limbs in a traction apparatus. Reduce the fracture at once so that the limb is restored to its correct anatomical position. By this means the vicious circle which initiates wound shock is broken. In my opinion it is a misconception that primary treatment should be delayed for the patient to recover from shock, hæmorrhage and swelling. All these conditions may be prevented or relieved by immediate reduction and control of the injured parts in correct position. With reduction of the fracture, there is restoration of the circulation and nerve supply; hence all the physiological functions of the injured part may be expected to improve. In the treatment of shock, an infusion is given of saline

glucose, whole blood or plasma, whichever is needed.

In fractures of the lower limb below the knee, I employ a Bohler's leg traction apparatus with a Steinman's pin through the calcaneus if necessary. For fracture of the femur, an orthopaedic table is used, or, if it is not available, a simple pelvic rest attached to an ordinary stout table will do. For the forearm I use fixed traction from a bracket in the wall to which a band is attached, and counter traction is made by an assistant on the forearm which is kept flexed to a right angle and in the mid-position of rest. As a general rule, I find that a minimal amount of traction is required in gunshot wounds, as the muscles are in a state of paralysis, and deformity is easily overcome; fractures of the arm are easily dealt with as the weight of the forearm is often sufficient to secure reduction and prevent displacement.

(c) *The wound*.—When the limb has been placed in the required position, the skin is cleansed with soap and water. The wound itself is covered with a dry sterile dressing, and the surrounding skin is thoroughly cleaned, working from the wound outwards. The hair around the wound for a distance of three inches is shaved, and the remainder is left. This is, I consider, important, as the hair is incorporated in the plaster of paris to be subsequently applied. It gives an even pull on the skin, and is comfortable. A shaven limb enclosed in non-padded plaster is uncomfortable. After the skin has been cleaned, ether is used; this is necessary often to remove oil or grease which nowadays is by no means an uncommon contaminant of the skin. Finally, any skin antiseptic can be used to complete the cleaning of the operative field. The limb is then draped and the operation proceeded with.

This consists in *excision and débridement*. The excision is the paring away of all devitalized and contaminated tissue around the wound track, as if the affected area was a tumour mass. To achieve this completely is impossible in practice except in the most superficial types of wound. The débridement is the surgical relief of tension by the division of fascia and muscle sheaths. It is not the removal of debris as is sometimes erroneously thought. This latter is more correctly called *épluchage*.

The skin edge all around the wound is removed for a distance of  $\frac{1}{2}$  to 1 cm., if possible in one piece, keeping the knife perpendicular to the surface. Next the subcutaneous tissue and fascia are excised with scissors, leaving a sharp continuous edge. When this stage is complete, easy access to the wound should be afforded; if not, the skin opening should be opened upwards and downwards; this is necessary in punctiform wounds. Foreign bodies, pieces of bullet, bomb, clothing loose pieces of bone and blood clot are removed. All ischaemic and necrotic muscle must be excised until contractile and bleeding muscle is encountered. It is here that the débridement is called for; fascial layers

and muscle sheaths will have to be divided and opened up to follow up retracted and damaged muscle. This relieves the constriction of the muscle masses due to swelling brought about by the concussion of the limb and subsequent tissue recoil. In the removal of the muscle, excessive mutilation should be avoided. In the deeper parts of the wound it will have to be done carefully lest vessels and nerves should be damaged. These should be seen if possible.

The fracture is next dealt with. All loose pieces of bone are removed. Those attached to healthy muscle or periosteum are left. The wound is completely 'saucerized' from top to bottom. Avoid as far as possible the use of catgut; secure haemostasis by forceps pressure or a hot moist saline sponge. *Divided nerves and tendons* are not sutured at this operation unless the wound is favourably situated and unless ideal conditions are present for primary closure of the skin wound. It is the rule of the surgery of warfare that *wounds are not closed by primary suture except in special cases*. These are in wounds of joints seen in the first six hours, in fingers, and in cases where the patient is not being moved and is under supervision for at least ten days. If the case has to be evacuated, remove the stitches and pack the wound. Total excision in severe wounds is an impossibility, as it always remains an incomplete proceeding and the end-result is always an infected wound. Short 'gutter' wounds are easily dealt with. Through-and-through wounds must be approached from one end and then from the other.

It is sometimes stated that through-and-through high velocity bullet wounds are relatively sterile and can be left alone. I do not agree that all should be left, as the small skin entrance and exit wounds are no criterion of the damage which may have occurred to the deeper structures. It is wiser to excise the skin wound and prolong the wound upwards and downwards and deal with the deeper layers as described. A good guide is the degree of tension in the limb after such a wound; moreover, if there is any suspicion of vascular damage, intervention is imperative.

In *wounds of blood vessels*, ligature is the procedure of choice under war conditions; such ligation should be performed at two points above the injury and the artery completely divided if it is not already so. Double ligation is preferable to ligature in continuity, since erosion of the vessel wall at the site of ligature is always a danger. When a large artery is ligatured in continuity, complete division permits retraction and shortening of the vessel due to its elastic contents, thus producing a thickened wall. Ligature in continuity also invites reopening of the ligature. Further, unless it is completely divided, it has been observed that vascular disturbances may develop years later, characterized by pain, poor pulse and claudication of the affected limb, symptoms which are completely relieved by division of the fibrous cord at the site of the previous ligature. According to

Leriche it is due to damage to the periarterial sympathetic plexus by the ligature producing a reflex vaso-constriction in the arterial bed distal to the ligature, thus obliterating or closing potential collaterals. The problem of whether ligature of the accompanying vein is desirable whenever a large artery is ligatured is still a subject of controversy. In my opinion the vein should be ligated. In a statistical summary it was found that among 995 ligations of the large arteries alone, gangrene occurred 154 times or 15.5 per cent and among 198 ligations of artery and vein, gangrene occurred 17 times or 8.5 per cent.

Injuries producing direct communication between artery and vein are inimical to the later health of the patient. The injury is accompanied by profuse but easily controlled bleeding, and by the prompt development of a thrill and bruit continuous throughout the cardiac cycles; occasionally these are delayed for several hours or days, due probably to temporary occlusion by a blood clot. The arterio-venous aneurism, if sufficiently large, will lead to cardiac dilatation and decompensation. To prevent this, operate under a tourniquet. Evacuate the hæmatoma and perform an excision and débridement. If the injured vessels are exposed in the absence of infection, a suture of a vessel might be attempted if heparin is available, but results are disappointing. If suture is not possible, the injured portions of the artery and vein are excised and the four ends of the artery and vein are ligatured with quadruple ligature and the wound is left open. Ligature of an artery alone proximal to a fistula is disastrous in that it leads to inevitable gangrene.

In concussion of an artery, localized segmentary spasm may occur. Treatment consists in exploration of the artery; division of the fascial covering and evacuation of a hæmatoma may succeed in relieving the spasm. If not, the intravenous injection of papaverine should be carried out; Griffiths (1940). Peri-arterial sympathectomy is not satisfactory. It is more satisfactory to block the sympathetic fibres to the limb by injecting 10 c.cm. of 2 per cent novocain around the pre-ganglionic fibres by paravertebral injection. In the upper limb this is done into the second and third inter-vertebral spaces; for the lower limb into the third and fourth lumbar spaces. In contusion with localized thrombosis, treat by ligature above and below the site, and excise the affected segment.

After the excision, débridement and reduction of the fracture, if present, the wound is *insufflated with sulphathiazole*. The wound is then *packed with sterile vaseline gauze*. No drainage tubes are used and the wound is not stitched even in part. The wound is packed wide open so that no pockets are allowed to occur anywhere. The pack must be carried to the depths of the wound and the vaseline gauze overflows on the surface of the skin for a distance of one inch so as to carry away the discharge from the wound. This vaseline gauze pack is then covered by a dry

sterile absorbent pad of cotton-wool. Trueta uses dry gauze instead of vaseline gauze. I have used this in a few cases but have given it up as I found that the granulations in the healing wound tended to become enmeshed in the interstices of the gauze and its removal at the subsequent change of plaster caused bleeding and breaking down of the granulation tissue.

The entire limb is then encased in an unpadded plaster of paris case without a window over the wound, and including the joints above and below the injury.

A similar cast is applied to wounds not complicated by fracture. It may be thought that the application of a plaster cast to the wound is unwise owing to swelling and œdema. On the contrary I find that the swelling and œdema are quickly reduced and pain and muscle spasm disappear.

*Infected wounds.*—Wounds seen over 8, 12 or 24 hours will be infected, and infection will vary in severity. Some will have mild infection; others will be grossly infected, with cellulitis, lymphangitis and osteomyelitis.

In these cases, reduce the fractures if present at once, so that the tissue planes are restored to their normal balance. The abolition of deformity and mal-alignment prevents pain, shock and muscle spasm.

Then open up the infected area freely, remove sloughing tissue and loose pieces of bone. Pack the wound with gauze after insufflating with sulphathiazole. Give a full course of sulphathiazole by mouth. The infection should be under control in 24 to 48 hours and the limb quiet. Then enclose the limb as previously described in a plaster of paris cast.

In neglected soft tissue injuries alone in which suppuration and cellular infection has occurred, open up the infected area with a liberal incision so designed as to reach the infection area between the muscle planes. If this is not possible, open through the muscle. The limb is then dealt with as previously described. After the first change of plaster in about 10 days or later, the limb is quiet and there are clean granulations. Secondary suture has been recommended, but I do not find it satisfactory, as the stitch tracks tend to become infected and they tear out; but place the limb in a zinc gelatine paste bandage after insufflation of the raw area with sulphathiazole and immobilize in a half plaster shell. Two applications of the zinc gelatine bandage are all that may be necessary (see figures 2 and 2a, plate XVII).

The prevention of gas gangrene depends primarily on early adequate surgery. It is to be remembered that certain predisposing factors give rise to its development, and the organisms of the anaerobic group have been cultured from war wounds in which there was no clinical evidence of gas gangrene infection. These factors are extensive laceration of muscle, circulatory disturbances sometimes caused by prolonged use of the tourniquet, the presence of foreign

bodies or blood clot, and inadequate drainage of deep penetrating wounds.

The argument has been brought forward that the closed plaster technique of Orr (1929) brings about anaerobic conditions. This is not so, as the injured extremity is immobilized in the correct anatomical position. There is restoration of the circulation and nerve supply, and adequate drainage, so that oxygenation of the tissues and the internal respiration of the damaged part is restored to normal.

Where gas gangrene has developed, immediate operation is imperative. The affected limb is opened widely in the longitudinal axis of the limb. If the limb has been sutured, sutures are removed. Two or three other incisions may be needed. All infected muscles are removed. It is sometimes possible if one muscle only is affected to remove it completely. In the removal of such a muscle, care has to be exercised that the blood supply to neighbouring uninfected groups of muscle is not interfered with. The wound is then irrigated with hydrogen peroxide. No dressings are placed in the wound. It is left completely open to the air. A gauze cage covers the area somewhat similar to that shown in figures 3 and 3a (see plate XVII). Full doses of sulphathiazole are given by mouth, and 10 to 20,000 units of polyvalent gas bacillus antitoxin are also given. In 10 to 14 days the limb can be enclosed in a plaster of paris case and then in a gelatine gauze dressing as described for dealing with cellulitis in the soft tissues. If there is a fracture, continue with the closed plaster treatment.

If the infection is not controlled or if the case is received in a condition in which it is obvious that this treatment will be of no avail, immediate guillotine amputation above the limb of infection will be necessary to save life. In more extensive involvement of a limb, e.g. in the lower limb where a case is received with involvement as far as the groin, nothing will avail.

After the guillotine amputation, put one or two tension stitches over the raw stump to keep the skin edges and muscles from retracting, having first applied sulphathiazole powder to the stump; then vaseline gauze is applied and the limb is immobilized in a plaster cast. This prevents fluid loss and avoids painful dressings. As soon as possible, perform a flap operation to make a good stump, as guillotine amputation cases do not do well. It is a life-saving procedure and nothing more. Certain amputations are condemned as unsuitable in Europe, e.g. Symes, Lisfrancs. It is however to be remembered that our patients in this country will find a Syme or Lisfrancs amputation more suitable and to their liking than an amputation at the usual site of election below the knee joint.

In wounds of joints seen in the first six to eight hours, it is my practice to excise the wound track and remove loose pieces of cartilage, foreign bodies, etc., and the wound is sutured provided that the case is not being evacuated.

If it is evacuated, remove the skin stitches and pack with gauze.

The whole limb is immobilized in a plaster of paris case, thoraco-brachial in the case of the shoulder and spica for the hip.

In the knee joint I have had satisfactory results in cases seen within the first six hours by closing the joint after stitching and immobilization in plaster.

In knee joints in which infection is present the joint should be opened by an incision extending up from the medial side of the patella and a finger's breadth from it so as to open up the suprapatellar pouch. A counter incision is made along and above the tendon of the biceps. The joint is washed out with saline and a limited excision is done. The wound is packed with vaseline gauze and the patient is put on a full course of sulphathiazole. You will know within 24 hours if the patient can retain his limb, by his general condition; locally the glands in the groin should have subsided and the limb will feel comfortable under the plaster. If not, amputation is indicated.

Wounds of the hands should be treated with extreme conservatism. During the period of contamination, wounds of the fingers are excised, the tendons stitched and bone fragments replaced. Traction is secured by adhesive tape or wire through the pulp. This is attached to Kramer wire incorporated in a plaster splint. No dressings are applied to the wound but a gauze cage is applied to the whole extremity (see figures 3 and 3a, plate XVII).

In infected cases I apply the vaseline gauze technique as is the case in other regions. In injuries of the carpus, removal of a bone or bones may be necessary. Never be in a hurry to amputate the hand in the more severe types of wound. Any one who has seen an individual without a hand and one with a partial hand or even one finger can have no doubt as to the efficiency of the latter over the former (see figure 4, plate XVII).

Wounds of the foot can be very resistant to treatment. Wounds of the talus and calcaneus keep discharging for months as a result of a low-grade osteitis. An excellent operation I have found in dealing with chronic osteomyelitis in the calcaneus is Gacnslen's (1931) which is as follows: The heel is incised in the midline from the attachment of the tendo achillis to the anterior extremity of the os calcis on the plantar surface. The structures are dissected to the bone, the plantar artery, vein and nerve being avoided in the distal end of the wound. With a broad osteotome, the os calcis is divided in half, proceeding obliquely from the posterior and plantar surfaces. The two halves are retracted exposing the interior of the bone. All sequestra and obviously infected material are removed by curettage, the cortex being left as intact as possible. Soft tissue and sinuses on the medial or lateral aspect of the heel are likewise curetted. The wound is packed open with vaseline gauze.

The after-treatment consists of a plaster of paris boot case. As a rule, plantar scars are painful on weight bearing, but this is not true following the Gaenslen incision. After healing is complete, the scar is so deeply placed that the edges of the incision curl inward forming a thick cushion on each side (see figure 5, plate XVII).

### *Plaster of paris*

The advantages of the closed plaster treatment over other methods according to Trueta are as follows :—

(1) Rest and immobilization allow local venous and capillary thrombi to form; these prevent and delay the spread of infection and are not broken down by repeated handling.

(2) Rest allows new capillaries to form which are not broken down by repeated dressings of the wound.

(3) The plaster maintains a constant beneficial pressure.

(4) The mixture of organisms on the wound by their mutual antagonism prevents the victory of any one group.

(5) To leave the wound uncovered as advocated by Schede and Bohler is good treatment for superficial wounds, but in deep wounds the dehydration and loss of heat which result from this treatment induce a condition of shock.

(6) The patient does not need constant dressing, adjustment of dressing and splints.

(7) The patient can often evacuate himself. He is mobile.

Finally there are very distinct advantages in mixed traction as against elastic traction. In the latter an amount of movement is impossible to avoid which is an irritant to the injured parts causing muscle spasm. In such a case the fractured surface is never under proper immobilization. Irritation of the wounds and inflammatory complications are common and frequently occur and this when coupled with the constant inspection and dressings of the wound which are carried out, the dice is loaded against the patient's chance of recovery.

With the plaster of paris case, immobilization is complete, muscle spasm is overcome and, if the wound has been dealt with adequately surgically, drainage is satisfactory and secondary infection and repeated assault on the healing tissues are avoided. When this immobilization of the bones and tissues is adequate, accurate and prolonged healing is, in my experience, sure. There has been no case of non-union in my series of 274 cases. Finally the patient is immobile. This is an important point in evacuating a hospital, say, in an air raid. He has no cumbersome splints or traction devices to require constant care and attention, and it is easier to look after in a small hospital with a limited trained staff.

I will not go into the full details of the application of the various plaster cases as these should be thoroughly understood by any one carrying out the closed plaster treatment of wounds, but I would comment on the following points :—

Plaster of paris bandages should be made with gauze of a suitable mesh. If the gauze is too thick in mesh or starchy, it is impossible to prepare suitable cases and they are apt to crack.

The plaster should be creamy and should contain no grit or lumps. One specimen of plaster

I was supplied with effervesced on the addition of water.

A good plaster must immobilize well and can only do so if it is skin tight. The hairs of the limbs are unshaven as they are incorporated in the plaster, and an even tension is thus exerted on the skin without discomfort. A shaven limb is uncomfortable in a plaster of paris splint. Padding must be placed over the bony points, on the acromion and iliac crests in the thoraco-brachial cases, on the anterior superior iliac spines and sacrum in hip spicas. A fillet should also be used to protect the gluteal fold, as this area is liable to be cut into by the plaster. A plaster case must also immobilize the joint above and below the injury. I also incorporate, under large spicas and thoraco-brachial cases, four tapes at each quadrant, which can be moved to and fro by the patient or his attendant. It is invaluable as it helps to relieve him of the itching which may occur under the plaster. This tip I have had from Colonel J. P. Huban, I.M.S. I also cut windows in these cases after having strengthened them with metal rods incorporated in the plaster at each quadrant. This is necessary in the hot weather. These windows are of course not over the wound (see figures 6, 6a, 6b, 7, 7a, 7b, 8, 8a, 8b, 9, 9a and 9b, plate XVIII).

Another difficulty in the hot weather is flies. There are few hospitals in India where these can be avoided. They tend to lay eggs under the plaster if the edges are not protected by gauze attached to the plaster edge and the skin, and secured there by sticking plaster. In the very severe hot weather, when the patient is doing well, I transfer him to a higher altitude where the climate is not so trying. He reports to the headquarters hospital once a month for an x-ray check or change of plaster when necessary.

After the application of the plaster of paris case, the patient is relieved of severe local pain and shock, and there is a striking difference in his general appearance. The drawn expression disappears. The temperature and pulse rate begin to fall to normal and this generally within from 48 to 72 hours in early cases. In later cases, for five to six days the temperature and pulse will be elevated. Locally the case becomes soaked with pure blood at the site of the wound, assuming a brick-red appearance; this is a favourable sign. There is no pain or local discomfort. Swelling decreases in the limb, and there is a good circulation and free range of movement in the fingers and toes. In the delayed case so treated, the swelling of the regional lymph glands subsides and the leucocyte count falls. A few days later, an unmistakable smell is noticeable. The elimination of this unpleasant feature has taxed the efforts of many; charcoal bags, laevulose solution incorporated in the jelly, soaking the bandages in perchloride solution have been tried. The latter I use coupled with eucalyptus oil and chlorine water



occasionally sprinkled on the plaster, but so far there has been no satisfactory remedy.

In a case not progressing satisfactorily, what are the signs and symptoms which warn one that all is not well? Despite the fact that the wound cannot be seen, general and local signs will indicate that all is not well. The general signs are a rise of temperature and pulse rate. Before jumping to erroneous conclusions, eliminate malaria. The total leucocyte and polymorphonuclear count is up.

Locally there will be a sensation of heat and tension in the wound, and the discharge from the wound into the plaster will be excessive and finally the local regional lymph glands will be enlarged and tender. An x-ray should also be taken; this may show mal-alignment of the bones or perhaps an area of bone necrosis with sequestration causing inadequate drainage. These findings will necessitate the removal of the plaster for re-alignment of the bone or for removal of sequestra for more adequate drainage. Cellulitis may be present and this will need incision and opening up of the tissue spaces. I have found that this occurs oftener in delayed cases. On removal of the plaster, the skin may show a dermatitis which is of no consequence as it is due to irritation of the skin by the discharge. An ointment of zinc oxide can be rubbed on the area. Changes of plaster should be done in the operation theatre and re-dressing done with all aseptic precautions.

A more serious complication is the development of gas gangrene underneath the plaster. This will usually declare itself quite early after the application of the plaster. When this is suspected, the plaster should be removed at once. I have luckily had no case develop.

*Secondary hæmorrhage.*—I have had one case and a description of this case will more clearly illustrate the signs and symptoms of this.

A sepoy was admitted with a bullet wound of the left calf in March 1939 which guttered the back of the tibia but did not fracture it. It progressed to fracture the fibula. The bullet was of the tribal variety and the casing had disintegrated.

As thorough an excision and debridement as possible was done, hæmorrhage was controlled and all pieces of the metal, as far as possible, were removed, the wound insufflated with sulphapyridine packed with vaseline gauze, and the limb encased in plaster of paris. Progress was satisfactory until the 17th day when the patient complained of a severe tearing pain in the limb which came on suddenly. There was a rise of pulse rate to 120 per minute. The plaster stain showed signs of fresh blood. Within half an hour the patient was removed to the theatre with a tourniquet applied, and the plaster removed. The vaseline gauze plugging had been practically pushed out of the wound. It was removed, the limb was cleaned up and the wound mopped dry and explored. It was seen that the posterior tibial artery was ruptured and ragged in appearance for about  $\frac{1}{2}$  inch. It was ligatured proximally and distally, the wound was repacked and the limb was replaced in plaster. His recovery was uninterrupted with the retention of his limb.

Persistent discharge and sinus formation indicate the presence of a sequestrum or other foreign body. The commonest cause I have found to be

a small sequestrum which does not appear to unduly delay union, as the closed method controls the sepsis and the hyperæmia which would militate against calcification of the callus.

*Syphilis* is a common cause of *non-union* of fractures in this country. In my cases as a routine, a Wassermann test is done. A study of x-ray films will often show signs of gummatous periostitis, and treatment should be begun at once.

*Avitaminosis.*—Many of my civil cases were in an extremely debilitated state as the result of malaria, chronic dysentery and low nutrition. The usual treatment for these diseases was given and, for the avitaminosis, a liberal diet was given. Recently I have given vitamin C by injection and by the mouth in cases in which at the first change of plaster the granulations appear pale and anæmic and there is a little apparent callus formation, or in which obvious signs of sub-clinical scurvy exist. This vitamin is important in the maintenance of intercellular cement substance so necessary in the healing of wounds. It is also important in calcium metabolism. These two functions are necessary in the repair of bones. One course is given so as to raise the body content of the vitamin if apparent pre-clinical scurvy is present. A high vitamin diet is then maintained.

*Treatment and prophylaxis of infection.*—Of the three sulpha drugs generally in use, sulphanilamide, sulphapyridine and sulphathiazole, the latter is by far the most potent against the streptococcus and has some effect on the staphylococcus. Its solubility in wounds is greater than that of sulphapyridine when employed locally. Up to 5 or 10 grains can be implanted locally. Orally 27 grammes can be given over a period of six days. For the past two years I have been using sulphathiazole, for the reason given above, and clinically I find the patients tolerate it better. There were none of the minor toxic symptoms seen which are commonly encountered with sulphapyridine. I found that my cases which were treated in the first six to eight hours were no better off than before I had adopted this treatment, but in delayed cases where a cellulitis was established it was invaluable in controlling infection. A perusal of the literature leaves one in a state of perplexity as to what is the correct procedure. The relative merits of these drugs used in prophylaxis are debated, and at present there appears to be no unanimity of opinion. In laboratory studies, these drugs are proved to have value, but the rather enthusiastic clinical adoption of local sulpha therapy has so far failed to provide conclusive evidence of the extent to which such prophylactic treatment has prevented the growth of organism in wounds. In my cases I use both sulphathiazole and polyvalent anti-gas gangrene serum for the following reasons. The sulphathiazole is bacteriostatic and may inhibit toxin formation, but there is no good evidence to show that the drugs can permanently neutralize or



inactivate bacterial exotoxin in the tissues. For this reason I would give anti-gas gangrene polyvalent serum as well in the treatment of gas infection.

Many authorities are sceptical about the value of gas gangrene serum, notably Bohler and Trueta who do not use it. I believe official opinion in England is sceptical. It is certainly true that the experience of the last war left grave doubts about the value of antisera in the treatment of established cases of gas gangrene. The value of serum when administered to wounded individuals as a prophylactic measure was not tested, and I am afraid this will now not be done owing to the incursion of the sulpha group of drugs. Experimentally the sulpha group of drugs have been proved inferior to antisera in the prophylaxis of gas gangrene. I use both, and administer the serum always by injecting it near the wound. In the present state of our knowledge I consider it justifiable in the interest of the patient to use both.

In my consecutive series of 274 cases in North Waziristan, I have had no deaths, and no case of gas gangrene or tetanus. There was one case of gangrene due to damage of the popliteal artery for which an amputation was done.

#### Acknowledgments

I am grateful to Colonel J. P. Huban, O.B.E., I.M.S., Inspector-General of Civil Hospitals, N.-W. F. P., for his permission to publish this article and to Dr. Abdul Raziq Khan, for help with the x-ray pictures.

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#### DESCRIPTIONS OF ILLUSTRATIONS PLATES XVII AND XVIII

- Fig. 1.—A gunshot fracture of the humerus showing disruption of the bone with the fragments displaced into the surrounding muscles.  
 Fig. 1a.—Union after 6 months, a small sequestrum present. Sound union occurred at 9 months.  
 Fig. 1b.—Case under treatment in a thoraco-brachial cast in full abduction, necessary as the weight of the limb would have caused distraction of the fragments and non-union.  
 Fig. 1c.—Showing union with a small sinus through which a small sequestrum was removed. Final result gave full flexion of the elbow joint except for the last ten degrees.  
 Figs. 2 and 2a.—Neglected bullet wound of the soft tissues treated by incision and drainage. Healing obtained by zinc gelatine bandage and immobilized on half plaster splint. More satisfactory than secondary suture in this country.

Figs. 3 and 3a.—Bullet wound of the thumb with fracture and rupture of the extensor tendon, primary suture and traction. The whole treated in a gauze cage. Stitches removed on the 7th day. Union of the fracture was secured at 4 weeks, final result perfect.

Fig. 4.—Shell wound of the hand causing ablation of the four fingers. Stump trimmed and placed in plaster of paris. More satisfactory than amputation of the forearm.

Fig. 5.—Result of a Gaenslen operation for a low-grade osteitis following a bullet wound. Result excellent. Bone healed, and the patient walks and runs without pain.

Fig. 6.—Showing thoraco-brachial cast with four tapes between it and the skin at each corner which can be moved to and fro to relieve skin irritation.

Figs. 6a and 6b.—X-ray of figure 6 showing fracture and healed result after 7 months' immobilization.

Figs. 7, 7a and 7b.—Gunshot fracture of the femur being treated by the closed method in a hip spica. Fig. 7a: X-ray showing the fracture on admission. Fig. 7b: Healed result 9 months later. Sequestrectomy was performed once during the course of the treatment.

Figs. 8, 8a and 8b.—Fig. 8 showing a fracture of the ulna with severe soft tissue damage as a result of a bomb. Plaster stained satisfactorily. Fig. 8a: Healing edges of the wound after the first removal of the plaster. Fig. 8b: Healed result in 10 weeks.

Figs. 9, 9a and 9b.—Showing gunshot fracture of the tibia and fibula (fig. 9); the case in a walking plaster after 3 weeks (fig. 9a); healed result in 16 weeks (fig. 9b).

## Medical News

### MEDICAL EDUCATION IN INDIA

IN India it is not often that we hear of any criticism of the system of medical education, and we therefore welcome Dr. K. V. Krishnan's presidential address on the subject before the Medical and Veterinary section of the 31st Indian Science Congress, 1944. We give below a summary of his main points.

India has a dual standard of medical education—a lower one for the licentiates and a higher one for the graduates. Hoping that the former will be abolished in near future, the lecturer proceeded to say that India with a population of 388 millions has 37 medical institutions and 42,000 doctors, but according to Western standard she should have at least 400,000 doctors, or ten times the present number. As the medical schools and colleges are jointly producing only about 1,700 new doctors in a year, there seems to be no hope of solving this question of inadequacy unless a way is found out to hasten production.

Despite the fact that all medical colleges are affiliated to universities, the outlook of most of them, if not all, is still to produce the 'tradesman doctor' who can prescribe a bottle of medicine or use a surgical instrument for the cure of disease. The majority of the doctors are averse to settling down in rural areas where 95 per cent of the population live and receive little or no medical aid; the few that do are unable to cater to the special requirements of the rural people and to adapt themselves to the condition of the villages for long. Although the majority of our graduates compare well with those of other universities, the average standard of the profession is not as high as it should be, the education of most of our

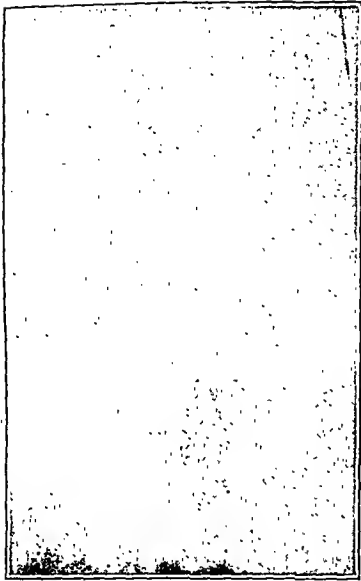


Fig. 1.



Fig. 1a.



Fig. 1b.

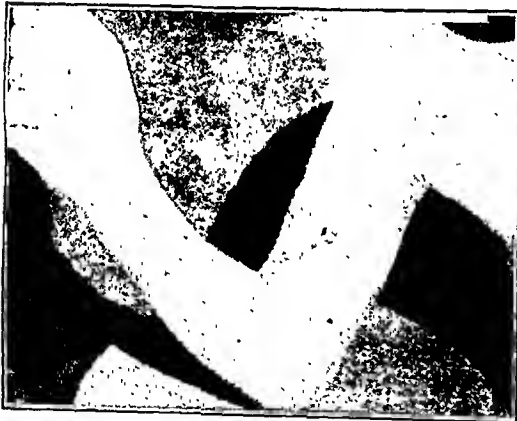


Fig. 1c.

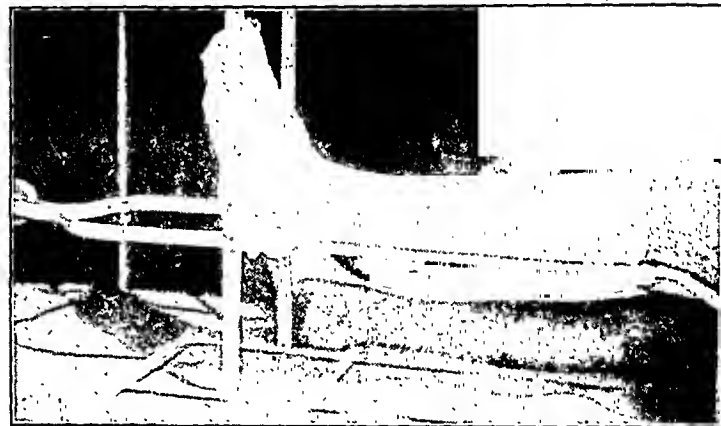


Fig. 2.

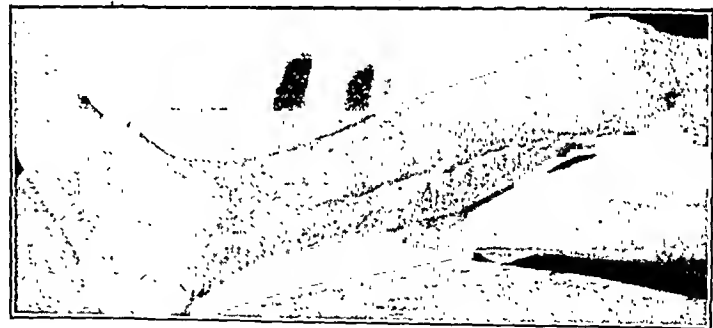


Fig. 2a.



For description see page 330.



Fig. 6.

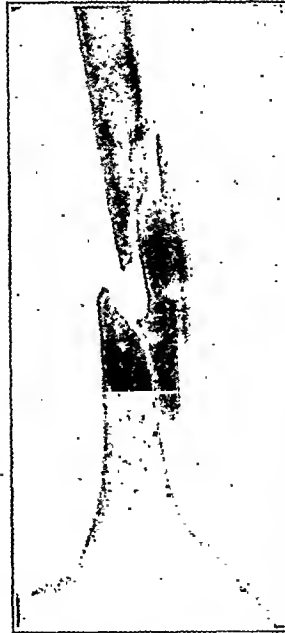


Fig. 6a.



Fig. 6b.



Fig. 7.



Fig. 7a.



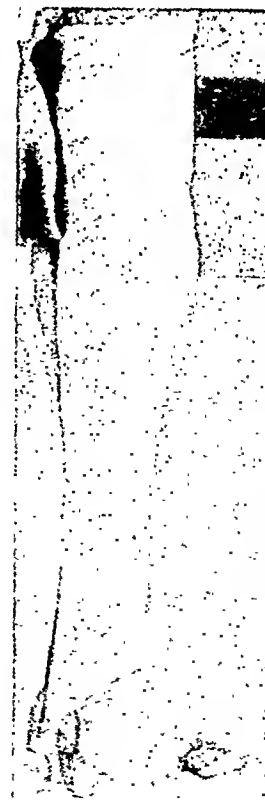
Fig. 7b.



Fig. 8.



Fig. 8a.



medical men practically ending with graduation. There is no proper organization for post-graduate training particularly for the general practitioner, and most colleges have only limited resources for prosecuting research. Although the importance of providing clinical facilities is recognized, the level reached by the best Indian medical college is the same as the level obtained by the lower ranking medical colleges in U.S.A., and in the medical schools conditions are very unsatisfactory in the majority of instances. The library facilities leave much to be desired, and libraries are mostly used by students who have no textbooks of their own.

#### The staff

Men with high qualifications, teaching and research experience, originality and initiative should alone be selected. Security of tenure, a good starting salary and good future prospects contribute to the efficiency of the staff. Two reforms are urgently required—the first is to debar the entire teaching staff from engaging in private practice so that they may give undivided attention to their duties. Hankering after private practice has been mainly responsible for low educational standard; moreover by virtue of the post they are in, they readily obtain certain free facilities and thus obtain an unfair advantage over the independent practitioners who cannot get them except at prohibitive cost to their patients. The second reform that is needed is to constitute a cadre for the teaching staff. At present the college staff form part of the provincial medical cadre and as such are liable to be transferred to non-teaching posts and replaced by men who may have no aptitude for teaching. In the teaching cadre it should be possible for the lowest member to aspire for the highest post in course of time. As far as possible, honorary men should not be appointed to teaching posts for the reason given above, their proper place is in non-teaching hospitals, and they may even replace the paid government doctors in suitable places, care of course being taken that the hospitals for the poor are not converted into private nursing homes for well-to-do patients.

#### Students

The majority of our students do not study medicine with the right attitude. From an enquiry of a few hundred graduate students as to the reasons that led to their taking to the medical profession, Dr. Krishnan came to the following findings—the parent's choice 25 per cent; tried for admission elsewhere but secured admission to the medical college 15 per cent; relations were successful doctors 10 per cent; their classmates joined medical colleges 15 per cent; medicine was the most paying profession 30 per cent and medicine was a noble profession 5 per cent.

As already mentioned, more doctors are needed to meet the enormous demand. There is no dearth of young men desirous of taking up the medical course, but as it will be a long time before we can hope to be in a position to increase the number of colleges, we should consider the possibility of training two batches of students at one time through a system of shifts as in a factory. This is in Dr. Krishnan's opinion practicable, and it was in this way that Russia has been able to make good the great shortage of doctors that existed in that country after the last war.

The country's needs may be taken as three—urban need, rural need and the need for women doctors. The urban need may be said to be quite reasonably met by the type we are admitting and training. The rural needs are not being satisfied at all at present; we really want a large number of men with the dual qualifications in medicine and public health, a special knowledge of village problems and their solutions, and a genuine desire to work in rural areas, and Dr. Krishnan presents a tentative scheme for their selection: training and employment. India with her medical problems so closely intermingled with her social problems has also great need for women doctors whose present number is totally inadequate. The medical

colleges should throw open their doors freely to women and offer scholarships in sufficient numbers to attract the right type.

#### Training

After giving an outline of modern methods of training, the lecturer referred to the lack of development of hygiene departments, none of which has any practice field where they can take the students for demonstration and field work. Further, only recently has internship been recognized as a basic part of under-graduate training. It should be compulsory and not less than one year in duration. There should be an organization for giving post-graduate training which is a legitimate responsibility of the medical colleges. For lack of refresher courses the general practitioner's knowledge is rusty, his outlook is restricted and his standard is low. Practically all the universities offer M.D. and M.S., but the standard of these is not that of the better class British or American universities. Only about 60 graduates take the diploma course in public health in a year, this number is but a mere trifle in a country like India. The All-India Institute of Hygiene should really be functioning as research centre for problems of national importance although as a temporary expediency it may train public health personnel of the diploma standard as at present. Similarly the status of the Calcutta School of Tropical Medicine should be that of an advanced post-graduate school. India is a tropical country and tropical medicine should be the concern of the departments of medicine in our medical colleges. It would be highly desirable to make it compulsory for every woman doctor to take a diploma in obstetrics and gynaecology as the need for properly trained graduates in this subject is really great.

In conclusion Dr. Krishnan said a few words about *ayurvedic* and *unani* systems. Opinion is rather divided—some want to retain and encourage them, others feel they should be scrapped, and yet others adopt a neutral attitude. His own opinion is in favour of abolishing 'this antiquated, empirical system of medicine'.

Although all may not agree with all the views expressed by the lecturer, the address is stimulating and should attract wide attention.

#### 21ST ALL-INDIA MEDICAL CONFERENCE, CAWNPORE

We have received the following letter from the Secretary, Scientific Section of the 21st All-India Medical Conference, Cawnpore (Temple of Service, The Mall):—

'You must have learnt by now that the next session of your Indian Medical Association is to be held at Cawnpore during the next Christmas week. The members of the Cawnpore Medical Association have taken upon themselves the responsibility of making this conference a success counting on the full co-operation of the medical profession in India. As you well know that the most important side of the conference is its scientific section and the task of organizing this section has been entrusted to me and I have accepted this difficult task on the confidence of getting your full support and co-operation.

'Success of the scientific section depends entirely upon the co-operation of friends like you who are masters of your subject and by your learning and experience can impart much knowledge and thus help in the advancement of medical science and render great service to the suffering humanity.

'For the present we have selected the following subjects for which papers and discussions are invited:—

'Surgery, medicine, ophthalmology and ear, nose and throat, obstetrics and gynaecology, radiology, pathology and bacteriology, tuberculosis, nutrition and paediatrics. If you are interested in any other subject the suggestions would we welcome.'

## Public Health Section

SMALLPOX IN KWEILIN, KWANGSI,  
1940-1941

## AN EPIDEMIOLOGICAL AND CLINICAL STUDY

By T. L. SU, M.D.

Department of Public Health, National Medical College  
of Shanghai

SMALLPOX, which has almost disappeared in many countries, is still one of the chief communicable disease in Kweilin, the capital of Kwangsi Province, China. Since the outbreak of the Sino-Japanese War in 1937, that city has become one of the most important centres in Free China. With rapid improvements in transport by highways, air and water, sudden increase of population from less than 50,000 in 1936 to 251,096 in August 1941, through the large influx of immigrants from the war zone and occupied areas, and with the great shortage of housing, further aggravated by numerous air raids, it is easy for an epidemic disease to be introduced and to spread like a great conflagration. Furthermore, the preventive and curative services in the city are still very inadequate to cope with the present emergency situation.

The local health organizations are still in their infancy. The number of beds in two provincial and two missionary hospitals totals only 240 for a city of that size! An isolation hospital of 30 beds has been established in the city under the auspices of the Anti-Epidemic Corps of the National Health Administration.

As a result of these factors, the city experienced in 1940 to 1941, one of the most severe epidemics of smallpox ever known. The writer had an opportunity of making a record of 267 cases (147 in the Isolation Hospital and 120 in homes), which represents only a partial picture of the whole epidemic on account of the imperfect

tion of the human virus. In the city proper, there were only a few sporadic cases reported during these months. However, an outbreak of smallpox in epidemic form suddenly burst out in the city in September 1940. In the middle of the month, a woman patient, suffering from smallpox, was admitted to the Kweilin Isolation Hospital. According to the history, she had left Kweiping on 2nd September, 1940, for Kweilin via Liuchow. It took three days for her to travel by bus from Kweiping to Liuchow. On 9th September, several days after her arrival at Liuchow, she began to show signs of smallpox. In spite of her illness, she continued her journey and came to Kweilin from Liuchow by a night train, and then stayed for five days at her own residence in a small lane near the north-west gate of the city before she was admitted to the hospital. Fifteen days after her arrival at her residence, an unvaccinated child in the same house was found suffering from the same disease, the parents of this child refused isolation in hospital. Two weeks later, a similar case in the same lodging place was reported. Three days after the discovery of the third case, a fourth one was found in the neighbourhood. Later, several cases were found in the vicinity.

Three days after the woman patient mentioned above arrived in the city, a male adult developed smallpox. The source of his infection was not traced.

In November of the same year, the infection began to spread in the military camps and police stations inside and outside the city.

*Seasonal variation*

The incidence of smallpox cases was highest in the winter months (November, December and January) as shown by table I and diagram.

TABLE I  
*Smallpox cases with reference to seasons*

Month	1940				1941							
	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	April	May	June	July	Aug.
Cases ..	3	7	44	112	55	16	9	9	7	3	2	0
Percentage of total.	1.1	2.6	16.5	41.9	20.6	6.0	3.4	3.4	2.6	1.1	0.8	0.0

reporting system; and it may be worth while to make an analysis of the data available.

*Origin and course of the outbreak*

From December 1939 to January 1940, in the south suburbs of Kweilin, there was a small outbreak of smallpox initiated by the inocula-

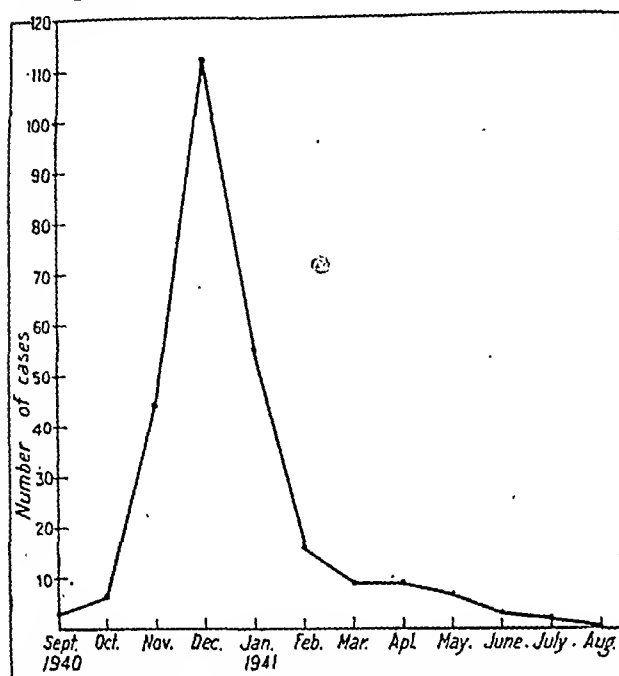
*Mode of transmission*

Smallpox is a disease transmitted chiefly by personal contact.\* The spread of infection is

\* Personal contact is said to be unnecessary for the transmission of smallpox. The infection is said to be frequently air-borne by droplet infection.—Editor, *I. M. G.*

related to the density of the population, as overcrowding gives more chance of contacts. In the civilian series of 204 patients, 41 gave a history

Diagram showing seasonal variation of smallpox.



The curve starts in September, reaches its peak in December, and declines gradually in the following months. If this curve represents the typical seasonal variation of smallpox in China, the old Chinese custom of vaccination against smallpox late in spring is apparently illogical. In order to prevent the disease in winter, the mass vaccination campaign should be launched in autumn instead of in spring.

of personal contacts with previous cases (table II).

TABLE II

*Smallpox transmission by contact*

Forms of contacts	Number of cases
1. Same family ..	7
2. Common lodging house ..	17
3. Close neighbourhood ..	13
4. Association through visiting a relative or friend.	4
TOTAL ..	41

*Incubation period*

It is difficult to ascertain definitely the length of the incubation period of the disease in this outbreak, as most patients belong to the uneducated class, and are not able to give a clear-cut history. However, there were 14 cases in which the date of exposure and that of onset of symptoms were known (table III).

TABLE III

*Incubation period of smallpox*

Number of days from exposure to onset of symptoms	Number of cases
4	2
6	1
8	1
10	3
12	3
13	3
16	1
TOTAL	14

The incubation period of smallpox was quite variable, ranging from 4 to 16 days, most commonly about 10 to 13 days. An incubation period of four days is extremely rare; it was found in two cases (unvaccinated) in this series.

*Morbidity and mortality rates*

Excluding soldiers and policemen, the population in Kweilin at the middle of the year under review was calculated by the arithmetic method as 212,853 with 126,580 males and 86,273 females. Out of this population there were 204 civilian cases of smallpox, the morbidity rate being figured out as 95.84 per 100,000 per year.

There were 48 deaths among civilian patients, a specific death rate among civilians being 22.55 per 100,000.

In a total series of 267 patients, there were altogether 58 deaths, the case fatality ratio thus being 21.7 per cent. This is a rather high figure which shows that this epidemic was of the toxic type.

*Occupational distribution*

In this series of 267 cases, the occupational distribution is as follows:—

Children 106 or 39.7 per cent, soldiers and policemen 63 or 23.6 per cent, coolies 64 or 23.9 per cent, house-keepers 25 or 9.4 per cent, and others 9 or 3.4 per cent. Unfortunately no record was available of the occupational distribution of the general population, and occupational groups cannot be calculated.

*Age and sex distribution*

The age distribution of smallpox cases varies with the vaccinal status of the population and is also affected by the periodicity of the epidemics. Table IV shows the age and sex distribution of the smallpox victims in this epidemic.

The youngest patient in this series was an infant under one month of age, and the oldest one was 53 years of age. Since the age distribution of the population is not obtainable, the specific morbidity and mortality rates of the different age groups cannot be calculated.



TABLE IV  
Age and sex distribution

Age group	CIVILIANS		Soldiers and policemen	Total number of cases	Percentage of total
	Male	Female			
Under 1 ..	15	24	0	39	14.60
1-4 ..	20	15	0	35	13.10
5-9 ..	8	10	0	18	6.74
10-14 ..	4	9	0	13	4.87
15-19 ..	16	8	9	33	12.34
20-29 ..	29	25	36	90	33.70
30-39 ..	11	6	18	35	13.10
40-49 ..	2	1	0	3	1.12
50-59 ..	1	0	0	1	0.37
TOTAL ..	106	98	63	267	100.00

Among the civilians, the morbidity rate was 85.74 per 100,000 for males and 113.59 per 100,000 for females. As the number of soldiers and policemen was not available, it would be rather difficult to prove that the morbidity rate was definitely higher in females than in males. With regard to the case fatality ratios, the figure for females (33.7 per cent) was significantly higher than that for males (14.8 per cent) as shown by table V.

TABLE V  
Sex and case fatality

Sex	Number of cases	Number of deaths	Fatality rate, per cent
Male ..	169	25	14.8
Female ..	98	33	33.7
TOTAL ..	267	58	21.7

#### Clinical and laboratory findings

Regarding the clinical and laboratory findings of the smallpox cases under this study, there were several points worth mentioning:—

1. *General clinical picture.*—The type of smallpox in this epidemic belonged to 'variola major'. Most patients showed serious symptoms, and deaths usually occurred in the second week, especially on the 11th and 12th days of the disease (table VI).

TABLE VI  
Time of deaths in smallpox cases

Death occurred in	Number of cases	Percentage of total
1st week ..	3	9
2nd " ..	21	62
3rd " ..	8	23
4th " ..	2	6

The earliest death in this series occurred on the sixth day of illness, and latest one on the 22nd day. The early deaths were usually due to toxæmia and the late deaths due to lowering of general resistance. Two hæmorrhagic cases with serious symptoms died soon after the onset of the disease.

2. *Urinary findings.*—Among the hospital cases, large quantities of albumin in urine were found in 10 per cent, and slight traces of albumin in 50 per cent. The amount of albumin in urine seems to run parallel with the severity of the general condition.

3. *Blood picture.*—Lymphocytosis is quite characteristic of the disease. In this series of cases, lymphocytosis was present even before pustulation, and persisted for some time after cicatrization began to occur, while during the pustular stage the total white count also increased (11,000 to 16,000) with a predominance of lymphocytes.

4. *Sequelæ.*—Among the recovery cases, one patient, having been treated at home, lost one eye from the infection, while the rest showed no sequelæ except the permanent pitting of the skin.

#### Relation of vaccination to smallpox

Among the 267 cases of smallpox, 91 patients had never been vaccinated, 123 had been vaccinated once in childhood, and 20 vaccinated twice in their lives. Thirteen had been inoculated with the human virus, while the rest were not able to give a reliable history of vaccination. As brought out by Greenwood (1935) there is no close association between the social status of patients and the fatality of smallpox; to evaluate the protective effect of vaccination the fatality ratio would serve as a better index, as it eliminates the social factor. Table VII shows that out of 156 cases of the vaccinated group there were 19 deaths or 12.18 per cent, while in a series of 91 unvaccinated cases 34 cases or 37.36 per cent were fatal.

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As a result of these experiments (described in detail in the *British Medical Journal* of August 28th, 1937) Bovril emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

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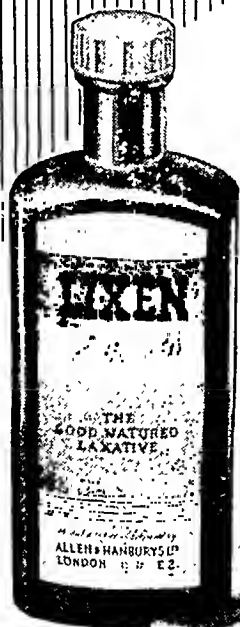
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TABLE VII  
*Fatality of the vaccinated and of the unvaccinated*

Age group	VACCINATED			UNVACCINATED		
	Cases	Deaths	Fatality, per cent	Cases	Deaths	Fatality, per cent
0-4 ..	14	2	14.3	58	23	39.6
5-9 ..	7	1	14.3	11	2	18.2
10-19 ..	29	5	17.2	10	5	50.0
20-29 ..	72	9	12.5	8	2	25.0
30-39 ..	30	2	6.6	4	2	50.0
40-49 ..	3	0	0.0	0	0	0.0
50-59 ..	1	0	0.0	0	0	0.0
TOTAL ..	156	19	12.18	91	34	37.36

(Twenty cases whose histories of vaccination were not known have been omitted from this table.)

Moreover, the age distribution of patients was quite different in the *vaccinated* and the *unvaccinated* groups as shown in table VII. In the *unvaccinated*, the greatest number of patients fell in the group under five years of age, and the number decreased as the age increased, while in the *vaccinated* the greatest number fell in the group of age 20 to 29. In other words, in the absence of vaccination, the infection of smallpox was obviously the highest in childhood, while among the vaccinated this period was passed in comparative safety. It also confirms what Hutt and Thomson (1935) have stressed that vaccination protects against the infection of smallpox as well as against death from the disease, and that the duration of protection conferred by vaccination against an attack of smallpox is very much shorter than that of its protection against death from the infection when contracted.

In this respect, the experience in Kweilin is in close conformity with that of Gayton and Camerson in England (tables VIII and IX).

#### *Hospitalization*

In dealing with a smallpox epidemic, hospitalization of all the cases should be insisted on. It is best for the patient, his family and the community. We should not be misled by the slightly higher fatality ratio in the hospital cases (23 per cent) in comparison with those treated at home (21.7 per cent), because most of the hospital cases belonged to the serious and late group.

#### *Control measures adopted*

It is a matter of deep regret that during the smallpox epidemic in the city, some of the essential measures, such as notification, isolation, and compulsory vaccination of the population, were not satisfactorily carried out for various reasons. A United Vaccination Campaign was launched by the existing health organizations in the city and about 10 per cent of the population consisting chiefly of school children were vaccinated in a period of about eight months. But many of the pre-school children and adults were overlooked. The existing facilities for isolation in this city were inadequate. Most patients

TABLE VIII  
*Fatality ratios of the age groups of the vaccinated and of the unvaccinated in smallpox as based on Gayton's experience in England (Greenwood, 1935)*

Age group	VACCINATED			UNVACCINATED		
	Cases	Deaths	Fatality, per cent	Cases	Deaths	Fatality, per cent
5-10 ..	945	61	7.30	510	180	35.29
10-15 ..	1,592	79	4.96	317	74	23.34
15-20 ..	1,848	117	6.33	204	86	42.16
20-25 ..	1,399	167	11.94	174	83	47.70
25-30 ..	834	127	15.23	105	56	53.35
30-35 ..	490	71	14.49	53	22	41.51
35-40 ..	320	70	21.88	50	20	40.00
TOTAL ..	7,428	692	9.31	1,413	521	36.87

TABLE IX

*Fatality ratios of the age groups of the vaccinated and of the unvaccinated in smallpox as based on Camerson's experience (Hutt and Thomson, 1935)*

Age group	VACCINATED			UNVACCINATED		
	Cases	Deaths	Fatality, per cent	Cases	Deaths	Fatality, per cent
0-10 ..	143	2	1.59	1,441	459	31.85
11-20 ..	1,218	23	1.88	761	166	21.81
21-30 ..	2,675	144	5.37	374	129	34.49
31-40 ..	1,861	247	13.27	180	80	44.44
41-50 ..	893	174	18.21	102	57	55.88
51-60 ..	311	55	17.68	73	31	42.46
TOTAL ..	7,101	645	0.08	2,931	922	31.45

were admitted too late to the Isolation Hospital, while the rest shunned isolation and there was a lack of legislative power. The course of this epidemic was apparently a natural one, not much influenced by vaccination and isolation.

#### Discussion

In view of the rapid means of transport in Kweilin, and the comparatively long incubation period of smallpox, it would be difficult for a quarantine station to detect cases among the passengers and to prevent the importation of the disease. Once the disease started in a city with a population of low immunity, it would spread like a great conflagration unless it could be checked by proper measures. In Kweilin, over-congestion of the population during wartime and the ignorance of the public of the importance of early primary and re-vaccination were additional factors in favour of spread of the infection.

In spite of the lack of proper control measures, the epidemic gradually died out in the city; this might have been due to several factors, among which the change in infectivity may be the chief one. According to Topley (1933), changes in infectivity do occur in the experimental epidemics of bacterial infections. Smallpox, being a virus disease, may be under the same category. Brownlee (1915) submits evidence in favour of a decrease in infectivity based on the character of the smallpox epidemic in London in 1901 and in 1902 which showed a centre of maximum intensity with a radiation of declining incidence.

The active immunization, naturally acquired or artificially induced, and the mortality selection might have played some rôle, but their effect in this epidemic would not be very much. However, the decline of the infection may be accelerated by a combination action of the above three factors, namely, change in infectivity of the virus, active immunization and mortality selection.

Sir Arthur Newsholme (1935) does not doubt that the old-fashioned name 'epidemic constitu-

tion' embodies a truth of magnitude. There is at present no way either to prove or to disprove it.

With regard to the future course of the disease in Kweilin it is impossible to forecast anything very definite. Probably, this disease will be present in the future in endemic and epidemic forms. The cycle of the epidemic expansion depends upon the virulence and infectivity of the virus, the change of the characteristic of the population, the degree of immunity conferred by vaccination and by previous outbreaks, the length of time lapse after the previous attack, and many other factors.

#### Recommendations

To prevent another epidemic of smallpox in Kweilin as elsewhere, the following are of importance:—

1. *Enforcement of mass vaccination.*—To increase the herd immunity in the population by means of mass vaccination is the best known method to prevent the prevalence of smallpox. Vaccination performed in infancy and repeated sufficiently often, will secure the individual the desired immunity against smallpox throughout life. According to the Chinese Vaccination Act of 1928, a child is required to be vaccinated against smallpox in two periods:—

(1) From the fourth month after birth to the second birth day.

(2) At the age of 7 to 8.

From the lessons in this epidemic, the writer is inclined to modify the Act as follows:—

(1) The first vaccination is required within the first six months of life.

(2) A second vaccination is required at the age of 6 (the age of entering school).

(3) A third vaccination is required at the age of 16.

To educate the public, a nation-wide vaccination campaign must be well planned and carried out at least once a year. For this purpose, a sufficient number of vaccinators, both lay and medical, must be trained, and free vaccine must be available to all. For rural areas, school



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teachers may be trained to act as public vaccinators. In the meantime, the old method of inoculation with the human virus must be abolished, as it often causes outbreaks of smallpox epidemic.

2. *Control of immigrants.*—In order to bring the smallpox infection under control, immigration must be carefully controlled. The immigrants who have failed to show certificates of vaccination of sufficiently recent date, must be vaccinated. Greenwood *et al.* have shown in experimental epidemic that a succession of epidemic waves of an infected herd can be maintained by the persistent addition, from time to time, of definite numbers of 'unsalted' immigrants.

3. *Avoidance of over-crowding.*—To reduce the chance of contact with cases of smallpox and other communicable diseases, overcrowding should be avoided. Therefore, a new city plan should be made with better housing conditions for the population.

4. *Early notification of cases.*—In order to have an early control of smallpox and other communicable diseases in a city, the reporting system must be improved and strictly carried out.

5. *Enlargement of the isolation hospital.*—The present facilities in Kweilin for isolating smallpox and other communicable diseases are too limited, and efforts should be made to establish a new and modern isolation hospital of 50 to 75 beds, preferably located not in a too thickly populated district, and to provide isolation wards in the existing hospitals in the city.

### Summary

An epidemiological and clinical study of an outbreak of smallpox in Kweilin disclosed the following:—

1. The epidemic rapidly rose from September 1940, reached its peak in December 1940, and then gradually declined toward the end of August 1941. The report is based on 267 cases studied.

2. For civilians, the morbidity rate was 96 per 100,000, and the specific death rate 22.55 per 100,000 in that year.

3. The fatality ratio was 21.7 per cent with a higher figure in the females (33.7 per cent) than in the males (14.8 per cent).

4. The case fatality was much higher in the unvaccinated (37.36 per cent) than in the vaccinated (12.18 per cent). This indicates that a better prognosis of smallpox can be expected among vaccinated than among unvaccinated.

5. The greatest number of patients fell in the group under five years of age among the unvaccinated, and in the third decade of life among the vaccinated. This fact points out the importance of re-vaccination in the adolescent period of life.

6. In this series of cases, the youngest patient was an infant under one month of age, and the oldest was 55 years of age.

7. Several secondary cases were traced to a primary case in a woman patient, and there were other foci of infection.

8. The incubation period of smallpox in this epidemic was variable, ranging from 4 to 16 days, most commonly about 10 to 13 days.

9. Clinically this epidemic belonged to the classical toxic type. Albuminuria and lymphocytosis were constant findings.

10. The decline of the epidemic might have been due to the change in infectivity of the disease, with the effect of active immunization and mortality selection.

11. Measures of control of smallpox were recommended.

### Acknowledgments

The writer is indebted to Drs. John B. Grant, Winston W. W. Yung, H. C. Hsu, Daniel G. Lai, and F. Y. Li for critical aids.

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## Current Topics

### Studies in Vitamin-B Deficiency With Special Reference to Mental and Oral Manifestations

By A. G. CLARKE, B.Sc., M.B., D.P.M.

and

F. PRESCOTT, M.Sc., Ph.D., A.I.C., M.R.C.S.

(Abstracted from the *British Medical Journal*, ii, 23rd October, 1943, p. 503)

#### PSYCHONEUROSIS AND DIETARY DEFICIENCY

WE have recently seen 17 cases of vitamin-B complex deficiency in patients treated primarily for nervous disorders. This represents 2 per cent of the patients seen by us in the out-patient department of the West End Hospital for Nervous Diseases. Originally they were mostly classified as suffering from functional nervous disorder, and with one exception were women. The parallelism between the manifestations of a deficiency of the vitamin-B complex and those of psychoneurosis is seen from the following list. All are likely to be met with in the psychoneurotic; those in italics may result from a deficiency of the vitamin-B complex.

General: *Fatigue, anorexia, indigestion, constipation, diarrhoea, dizziness.*

Circulatory: *Tachycardia, palpitation, shortness of breath.*

Vasomotor: *Pallor, blushing, sweating.*

Nervous system: *Headache, backache, insomnia, photophobia, hyperacusis, noises in the head, vertigo, hyperaesthesia, paraesthesia.*

Mental symptoms: *Inability to concentrate, self-consciousness, depression, phobias, anxieties.*

So close is the parallelism that early cases of pellagra—which is a multiple deficiency disease—are often diagnosed as 'functional' by those unacquainted with the early manifestations.

## The Treatment of War Wounds with Penicillin

(From the *British Medical Journal*, ii, 11th December, 1943, p. 755)

*The following is an account written for us by Prof. L. P. Garrod of a report published by the War Office entitled, 'A Preliminary Report to the War Office and the Medical Research Council on Investigations concerning the Use of Penicillin in War Wounds—carried out under the Direction of Prof. H. W. Florey, F.R.S., and Brig. Hugh Cairns, F.R.C.S., R.A.M.C.' This report is for official use only, but we are permitted to publish an abstract of its contents.*

THIS printed report of 114 pages is in two parts: a general account of the investigation and its results by Florey and Cairns, and 12 detailed descriptions of particular classes of case by individual surgeons, including numerous fairly full case histories. The work described was carried out in North Africa during a period of only 3 months last summer, in order to ascertain as quickly as possible how penicillin can be used to the best advantage in treating battle wounds. The best use of very limited supplies involved discovering how to obtain good results by local treatment only, since this is far more economical than systemic administration. No attempt was made deliberately to compare penicillin treatment with any other—a much more formidable project.

### METHODS OF ADMINISTRATION

Penicillin was applied locally either as a solution in distilled water containing 250 units of calcium penicillin per c.mm., as a powder in which calcium penicillin was diluted with sulphanilamide to give a strength of 500, 2,000, or 5,000 units per g. (in a few cases it was used undiluted), or as a cream in a lanette wax base. Systemic treatment was achieved by intramuscular or intravenous injection of sodium penicillin by continuous drip in glucose saline, the daily dose being usually 120,000 units: owing to impurities in some of the batches used injection by the former route caused pain and by the latter febrile reactions and early venous thrombosis. There were no serious toxic effects. A good plan was to give intramuscular injections for 1 day after operation, then start on intravenous drip, and revert to intramuscular injections later if necessary. Some loss of potency occurred, especially in calcium penicillin, owing to climatic conditions and transport: doses stated are therefore maxima and the probable true dose was up to 30 per cent less.

### CHRONIC WOUND SEPSIS

The first phase of the investigation was the treatment in Algiers by Lieut.-Colonel Ian Fraser of a series of septic wounds from 3 weeks to 4 months old. These cases were accommodated in a special 30-bed ward, and full bacteriological control was carried out by Major Scott Thomson. Local treatment with solution, powder, and cream was disappointing: accessible surfaces could be sterilized, but deep-seated infection could not be controlled. Systemic administration was resorted to in 8 cases of septic compound fracture, 4 of which received over 1,000,000 units; this lavish treatment cleared up the infection in 6.

It was concluded from this experience that long-standing sepsis with loculated abscesses and poor general condition was a relatively unpromising field, and that cases should be treated earlier. Almost ideal

arrangements for this were possible when the campaign in Sicily opened. Lieut.-Colonel Fraser and Major MacLennan (bacteriologist) proceeded to Sicily, where they examined casualties early and gave preliminary treatment: the men were then evacuated to Tripoli or Sousse, where 10 surgeons in 5 general hospitals who took part in the investigation worked in collaboration with Florey and Cairns. The cases treated were of 2 principal classes.

### RECENT SOFT-TISSUE WOUNDS

Of these there were 171, of which 53 were treated by Lieut.-Colonel J. S. Jeffrey: they were mostly from 3 to 12 days old (extremes 12 hours and 22 days), and the majority were infected, . . . in fact some were purulent and most were clinically dirty. No case was rejected for this reason, and the wounds were closed before the results of the preliminary bacteriological examination were known. Large and difficult wounds were chosen, including 25 of the buttock: 7 cases were amputation stumps. The policy adopted was immediate closure, relying on penicillin applied locally to hold infection in check. The principal method of application was through tubes inserted at the operation for suture. One or more 1/8-in. rubber tubes were introduced through stab holes or through the wound itself, the outer ends projecting beyond the dressing, and through these from 3 to 10 c.cm. of penicillin solution (250 units per c.cm.) were injected twice daily for 4 days. Some cases were also treated by insufflation of powder, either as a preliminary measure in the forward area (which according to Scott Thomson's bacteriological data reduced the frequency of infection with pyogenic cocci on arrival at the forward base from 57 to 26 per cent) or at the base for 3 days before closure was undertaken: powder alone with no irrigation after closure was used in exceptionally clean cases. Complete union was secured in 104 cases, subtotal union—i.e. healing by granulation in some part of the wound—in 60; failures numbered 7. These wounds show little reaction: they may remain dry or discharge 'a thin salmon-pink purulent fluid' which turns green on the dressing—this is 'Gram-negative pus' containing *Ps. pyocyanea*, and healing proceeds rapidly in spite of its formation. The results as a whole were such that Jeffrey goes so far as to say: 'With penicillin the obstacle of infection has been practically overcome', and it is estimated that from 3 to 6 weeks in hospital is saved. Causes of failure or subtotal union were: stitching up so tightly in layers that the solution could not penetrate the whole of the wound; placing sutures too near the skin edge; removing sutures too soon; injecting too much solution (3 c.cm. per tube was found better than 10 c.cm.), since this tended to separate the wound surfaces; and relying alone on powder before suture when this tends to be washed away by blood. The main difficulty in applying this treatment was caused by unduly drastic wound excision in the forward area; it is very strongly emphasized that this should be conservative, skin especially being spared. It is also stated emphatically that suture should not be attempted in the C.C.S., and that at the forward base where it is undertaken the man should remain until healing is complete.

### RECENT FRACTURES

A different method was adopted for compound fractures. There were 36 of these cases, mostly severe comminuted fractures of long bones: they were 5 to 14 days old on arrival at the forward base; 9 had been treated locally with penicillin-sulphanilamide powder and 27 with sulphanilamide only. The aim was to convert to a simple fracture by closure and so prevent chronic infection, and systemic treatment was considered necessary: the standard course was 100,000 units daily (by the 3-hourly intramuscular or continuous intravenous route) for 5 days. Only 31 of the wounds were capable of being sutured: complete union was achieved in 16, subtotal in 10, and there were 5 failures. Of the 6 cases not sutured, 5 healed by granulation rapidly without infection and 1 died of fat embolism.

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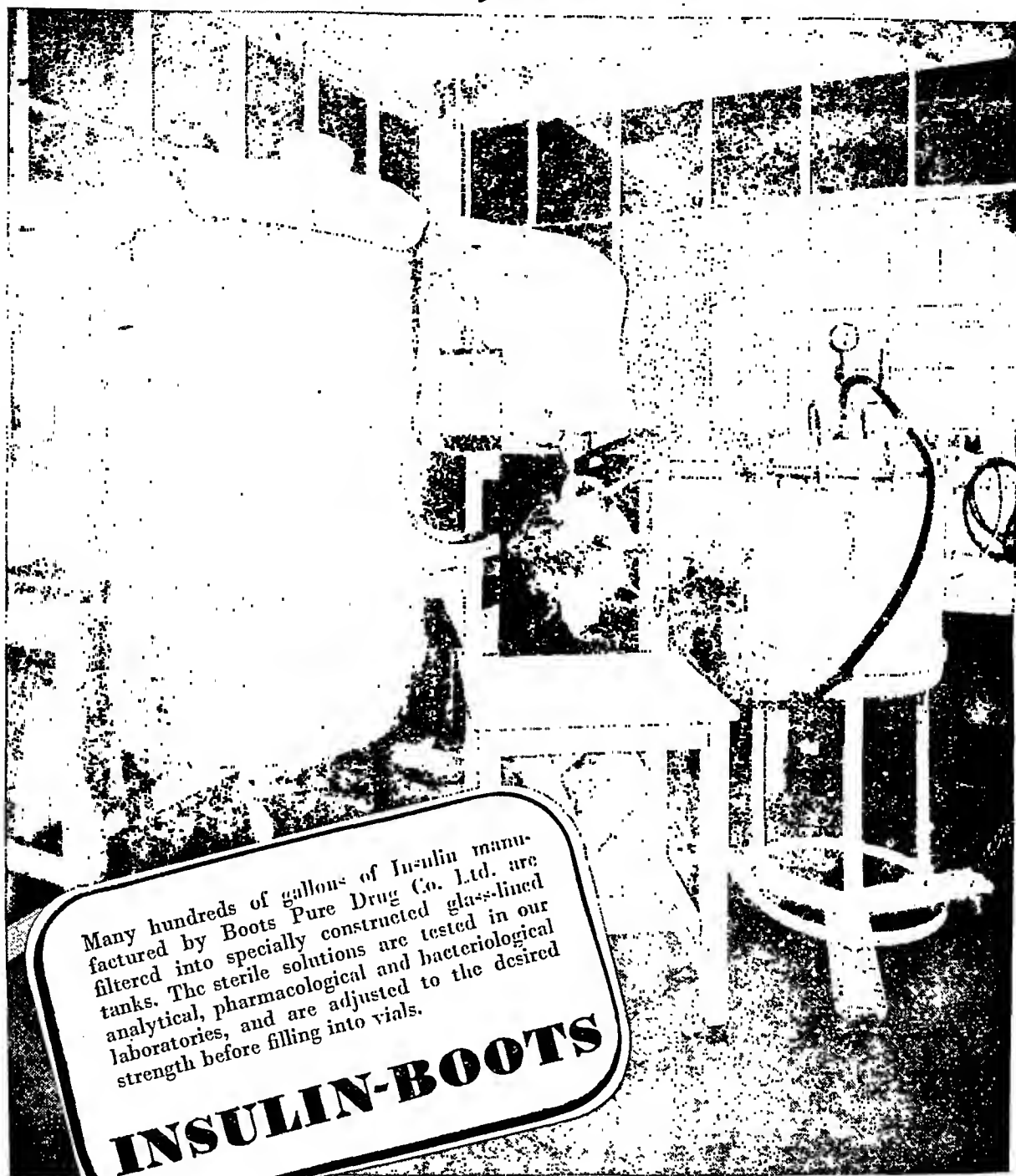
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Fractures of the femur gave the worst results, and it is advocated that in future systemic treatment for these should be continued for 7 to 10 days. Inadequate dosage was apparently the main cause of failure, and bacteriological studies showed that pyogenic cocci sometimes persisted after the full course. Closure was too ambitious in some of the large wounds, where drainage even for Gram-negative pus would have been preferable. There were also 2 examples of infection by penicillin-resistant cocci.

#### MISCELLANEOUS INFECTIONS

Smaller numbers of cases were treated in the following categories:—

**Gas gangrene.**—It was not often possible to get these cases to the forward base before they were moribund, but 7 cases were treated, of which complete histories are given. It is pointed out that the treatment should include full doses of antitoxin to combat the toxæmia, and the excision of all dead tissue, since penicillin cannot reach this. Systemic administration for 3 to 5 days is advocated: local application is useless in treatment, although it may be of great value for prevention. The infection was apparently checked in 4 cases: 3 died from causes apparently outside the control of penicillin.

**Head wounds.**—Brain wounds 3 to 12 days old, almost all infected with pyogenic organisms, were excised, cleaned, and closed: a small tube was passed through a stab hole into the brain cavity, and pus was aspirated and solution injected twice daily for 3 to 6 days. Of 23 cases only 3 died—2 of intracranial infection. These results, so far as they go, compare very favourably with those obtained by other methods. Most non-penetrating wounds of the skull and scalp were treated by a single application of powder at the time of suture.

**Undiluted powder and primary suture.**—During the first 2 days of the Sicilian invasion 13 casualties with wounds involving bones or joints in nearly all cases and averaging 40 hours old were operated on in a hospital ship off-shore. About 1 g. (50,000 units) of undiluted calcium penicillin powder was applied by spoon and rubbed into all parts of the wound, which was then closed. Results, so far as they are known, were excellent, but after-histories are not all available.

Some cases of burns were treated by insufflation with '1 per cent penicillin in sulphonamide powder': hæmolytic streptococcal infection was thus eliminated which had resisted other treatments. One recent and 9 sulphonamide-resistant cases of gonorrhœa were given not more than 12 4-hourly intramuscular injections of 15,000 units, the effect of which was 'like turning off a tap': no relapse was observed during 2 to 4 weeks' subsequent observation. (Sulphonamide-resistant gonorrhœa is common in N. Africa, possibly because French M.O.s in charge of brothels give small doses of sulphonamides to prostitutes as a prophylactic. The penicillin treatment of gonorrhœa should be restricted at present to highly trained fighting troops, such as parachutists, in forward areas.)

#### FUTURE POLICY

Evidence has been obtained that 'penicillin can make a substantial contribution to the health of wounded soldiers, with corresponding saving of hospital time'. Plans for its use should assume that an average of 750,000 units of sodium penicillin per case is required for systemic treatment and of 50,000 units of calcium salt for local. For the time being supplies should be under the control of the Directorate of Pathology at the War Office, and its use 'should be mainly concentrated in one theatre of operations'. Surgical and pathological penicillin officers should be in charge of treatment, which should be confined to predetermined types of case. The most hopeful field is the early treatment of soft-tissue wounds and fractures. Further experience should lead to improvements in technique, and only when the best methods have been defined should a comparison be made with forms of treatment

not employing penicillin. The appointment of a statistical officer is recommended, to supervise accurate record-keeping and a careful follow-up and to assess results. Similar information from an Army group not using penicillin would be valuable: there is an extreme dearth of accurate information about the frequency and duration of sepsis in battle wounds and the effects of other measures such as sulphonamide treatment. Among other types of case, gas gangrene requires further study, and penetrating wounds of the chest, which have hitherto been excluded, should be studied particularly with a view to discovering whether pyogenic coccal infection can be controlled by the more economical method of local application.

'There can be little doubt that the prevention of infection with pyogenic cocci or its control in war wounds is within reach, and no criticism with its emphasis on difficulties should be allowed to stand in the way of the attainment of this ideal.'

#### Antidotes to Arsenic

(From the *British Medical Journal*, ii, 27th November, 1943, p. 681)

THERE has lately been an increase in the number of patients suffering from symptoms of arsenical intoxication as a result of antisyphilitic treatment. The first published work which indicated the mechanism of arsenical poisoning was that of Voegtlin, Dyer, and Leonard in 1923: they showed that the action of arsenic on protoplasm was due to organic sulphur compounds containing the sulphur in the mercaptan or sulphhydryl form ( $-SH$ ). Neocarsphenamine is probably converted in the body into the arsenoxide form,  $R.As. = O$ , and Voegtlin and his colleagues showed that the action of arsenoxide on trypanosomes, both in the test-tube and in the living rat, was inhibited by adding sulphhydryl compounds such as cysteine or glutathione. Later the same workers demonstrated that the toxic action of arsenoxide for the rat itself was inhibited by the intravenous injection of glutathione in the reduced form. The toxic action was also lessened by feeding rats on a mixture of glutaminic acid and cystine, which are the constituents of glutathione. The conclusion from these observations is that when compounds containing sulphhydryl groups are administered, arsenic which is present in the body combines with these sulphhydryl groups rather than with the sulphhydryl groups of protoplasm.

These observations are probably related to the demonstration by Messinger and Hawkins in 1940 that a meat diet is very effective in protecting dogs against the toxic action of arsenic on the liver, and that a fat diet, on the other hand, conduces to toxic effects. For example, one dog eating a high fat diet became toxic and inactive with a high icteric index after the injection of 0.04 g. per kg. arsphenamine. When a protein diet was substituted the icteric index fell and the dog became active. Three more arsphenamine injections were then given, but in spite of these the bilirubinæmia fell and the dog remained well. It was then put back on the fat diet, when the icteric index rose from 2 to 21 units without more arsphenamine. A protein diet has similarly been shown to protect the liver of a dog against chloroform, and it is the sulphur-containing amino-acids in the protein which give the protection; it may be these amino-acids which protect against arsenic. It should be remembered that casein contains relatively much cystine.

A new approach has recently been made by Sandground and Hamilton, who were stimulated by the observation of Woods that *p*-aminobenzoic inhibits the action of sulphonamides on bacteria. Sandground and Hamilton wondered whether *p*-aminobenzoic acid would inhibit the action of pentavalent arsenicals such as tryparsamide on trypanosomes. They looked for this action, failed to find it, but discovered that *p*-aminobenzoic acid greatly reduced the toxicity of large doses of tryparsamide, carbarsone, acetarsone, and



other pentavalent arsenic compounds. For example, 1.5 g. per kg. carbarsone killed all rats; but if this dose was followed by oral administration of 0.75 g. per kg. *p*-aminobenzoic acid repeated twice on successive days, all rats survived. Some protective action could be demonstrated with doses so low as 15 mg. per kg. The protection afforded by *p*-aminobenzoic acid was greatest when it was administered either together with carbarsone or one hour previously; the protection was less if *p*-aminobenzoic acid was given after the carbarsone. Similarly, *p*-aminobenzoic acid gave good protection against arsenic acid if it was given three hours before. Sandground considers that the protective action is due to *p*-aminobenzoic acid interfering with the reduction of the pentavalent arsenicals to the arsenoxide form, inasmuch as *p*-aminobenzoic acid has very little protective action against the trivalent arsenical compounds like neoarsphenamine, or against arsenoxides like maphersen. Maphersen, it is interesting to note, is rapidly replacing neoarsphenamine as an antisyphilitic remedy in the United States; probably more than half the cases in the U.S. Army are treated with maphersen.

Still further work from another source has now been published. Goldstein, Stolman, and Goldfarb state that methyl chalcone of hesperidin reduces the toxicity of maphersen for rabbits. These workers were concerned to find a remedy for the encephalopathy which has occurred in 1.3 per cent of patients treated for syphilis with maphersen by the rapid 5-day method. Goldstein and Stevenson observed that maphersen in large doses damaged the brain capillaries of rabbits, and Goldfarb proposed the use of an aqueous extract of whole lemon to prevent arsenical encephalopathy. Lemon was believed to contain the factor diminishing capillary permeability known as vitamin P. Later a chalcone of hesperidin (a vegetable dye having vitamin P activity) was isolated from lemon peel, from which was prepared a methyl chalcone. Goldstein and his colleagues have now used this methyl chalcone in conjunction with maphersen, and state that it gives some protection against the toxic effect of large doses of maphersen. Maphersen in doses of 8 mg. per kg. twice daily for four days killed 13 out of 30 rabbits. If, however, the methyl chalcone was given intravenously daily for 7 days before and for 4 days during the maphersen injections, in doses of from 10 to 30 mg. per kg., then only 3 rabbits out of 30 died. These experiments are, however, still in the preliminary stage.

Of the three lines of work described, the first seems the one most likely to have a clinical application, though the second might also be tried. Both compounds, like cystein, containing sulphhydryl groups and *p*-aminobenzoic acid are fairly easy to obtain, and both might be tried, as remedies for arsenical dermatitis or for arsenical jaundice. Let us hope that this is being done.

### Shall Bassini Die ?

(From the *Lancet*, i, 8th January, 1944, p. 55)

MISGIVINGS about the results of operation for inguinal hernia have been increased by observations made in examining recruits for the Services. Both in hospital and in private practice the attempted cure of inguinal hernia is one of the commonest surgical procedures; but familiarity has too often bred inattention and the hernia operation has commonly been relegated to the end of the list when it is sometimes performed by assistants and house surgeons without guidance. Even before the war, it was known that the recurrence rate was high. Now Edwards tells of 805 recurrent hernias operated on during six months of 1942 in military hospitals alone, and he estimates that these probably represent only 60 per cent of the number presenting themselves in that short period. The original operations on these soldiers had been done—mostly in civil life—in all parts of Great Britain and Northern Ireland,

and were therefore representative of the results of British surgery as a whole. Operations on inguinal hernias in fit policemen in the wards of one of our foremost teaching hospitals have been followed by recurrence in as many as 12 to 20 per cent.

Faulty technique certainly accounts for a proportion of failures, and the time has come for surgeons to accept the fact that the operation is difficult and worthy of all their skill and patience. But the type of operation may also be at fault. Bassini's operation, or one of its modifications, is used almost as a routine, and its supremacy may not be justified. Changes have lately been discussed in our columns and elsewhere. For example, a modification of the Bassini operation, known by the name of McArthur, is upheld by McLaughlin, while Arther has further modified McArthur's operation. Arther stitches the conjoint tendon to Poupart's ligament, and reinforces the line of sutures by a fascial graft, dissected from the external oblique but not detached from it. He does not believe that simple removal of the sac is safe under Service conditions where subsequent abstinence from hard manual labour for a long time is impossible. Edwards, on the other hand, is strongly of opinion that, in the normal healthy male, removal of the sac, combined with repair of the tear in the transversalis fascia, is all that is needed; indeed he thinks that suture of the internal oblique and the conjoint tendon is destructive and should not be practised in such patients. During 19 months he and Capper personally operated on 131 recurrent hernias in men of military age. In 86 of them it was possible with reasonable certainty to say what was the original method of repair: in 53 this was the Bassini; in 19 the sac only had been excised; in 14 other methods, such as Bloodgood's, had been used. In cases treated by the Bassini operation the internal oblique was represented by a thin sheet of attenuated muscle, pale brown in colour. This finding supports the contention that suture of the internal oblique to Poupart's ligament is unphysiological, distorts the musculature, and by interfering with its contraction actually weakens the abdominal wall at the inguinal canal. Removal of the sac alone has long been the usual operation in children, where any further repair has been regarded as surgical interference; but dissection of the sac from its coverings must be complete, otherwise the stump will be an easy starting point of a fresh hernia. For adults this is recognized as the most important step in the operation; but where there is a gap in the posterior wall, some method of strengthening the inguinal canal must be devised. Discarding the Bassini type of repair, Edwards proposes a choice of two methods. One is to dissect a flap of the anterior layer of the sheath of rectus abdominis, which is then hinged downwards and attached with interrupted stitches to the upturned edge of Poupart's ligament; this he advises only for the infrequent direct hernia. The other is to darn the gap in the inguinal wall with a Gallie fascial graft.

Edwards is less concerned, however, with methods than with results. Hernia can be a grave disability, and working men often pay a heavy price for surgical failure. No one should be burdened through his best years with an unnecessary truss, and to most men radical cure of hernia at 30 is actually more important than radical cure of cancer at 70. The surgeon who takes care of the gastrectomies but leaves the hernias to take care of themselves shows a lack of proportion. It is now evident that 'routine' treatment of hernia cannot be relied on to cure the condition, and Edwards is right in urging that the patient with hernia presents a problem deserving thought as well as care. After operation active treatment is still needed. Three weeks in bed is required, but within a day or two of operation the patient should begin graduated exercises to restore muscle tone.

The custom in the Army is to provide three weeks in bed, three or four weeks in a convalescent home, and finally four to five weeks in a convalescent depot where eventually the soldier is restored to full physical efficiency before he goes back to his unit.

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 Glycerini m. 6  
 Chastim grs. 24  
 Chireta grs. 12  
 Gulancha grs. 12  
 Neem grs. 6  
 Myrobalans grs. 6



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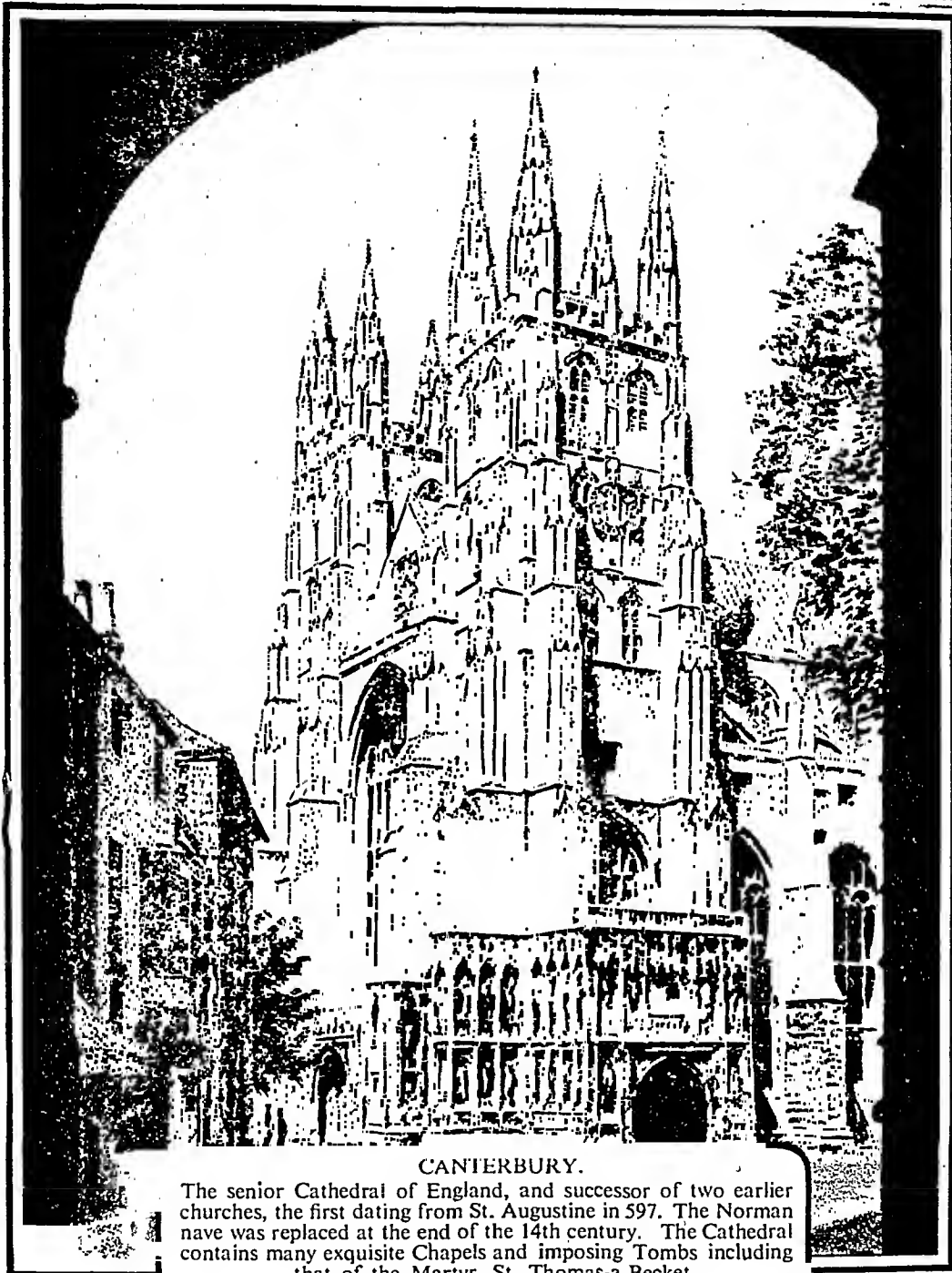
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## Digitalis in Cases Showing Normal Rhythm

By D. M. LYON

(Abstracted from the *Edinburgh Medical Journal*, Vol. L, December 1943, p. 746)

As a result of digitalization in patients with normal rhythm, pulse slowing was produced in 90 per cent of 180 trials.

The amount of slowing was proportionate to the rate of the heart at the time when the drug was begun.

Even where there is little or no effect on the pulse, diuresis and other clinical improvement may occur.

There would seem to be no justification for the belief that digitalis is only effective in cases of auricular fibrillation and in severe cardiac failure with normal rhythm.

## Viscose Tubing for Transfusions

By H. NAFTULIN

A. M. WOLF

and

S. O. LEVINSON

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIII, 9th October, 1943, p. 321)

### SUMMARY

THE cleansing of rubber tubing to be used for intravenous administration of blood or blood protein is difficult. Incomplete cleansing of rubber tubing is believed to be a major cause of pyrogenic reactions.

Heavy walled Viscose tubing is sturdy, pyrogen free, impermeable to pyrogens, impermeable to bacteria and quite practical for one time use.

In a total of 1,137 blood transfusions given through Viscose tubing the incidence of pyrogenic reactions was 0.64 per cent. This is a material decrease from the reaction rate encountered with rubber tubing.

## Reviews

**THE PRINCIPLES AND PRACTICE OF TROPICAL MEDICINE.**—By L. Everard Napier, C.I.E., F.R.C.P. 1943. Part I. Published by Thacker, Spink and Company (1933), Ltd., Calcutta. Pp. xii plus 522. Illustrated. (Obtainable from W. Thacker and Company, London.)

THE war upon disease will continue to be waged by the doctor to his life's end. Long after the captains and the kings depart from the present stricken fields of war, the field of medical research and practice will be fought over and will endure along with its subject mankind.

This volume upon the strategy and tactics to be employed against the enemy upon a major front in medicine, that of tropical disease, has appeared when such a work is most wanted.

Other and excellent textbooks of tropical medicine exist. This one has been written by one long in the field before, and still in it, during the briefer conflict in arms which in India, at all events, has greatly altered qualitatively and quantitatively various tropical diseases from their peacetime aspect; it has altered their distribution, racially by the influx of masses of British and American troops, and geographically by large troop movements.

Opportunity has occurred for the study of their impact upon new arrivals in the East unprotected by previous frank or subclinical attacks of disease.

Dr. Napier remained with us in India long enough to benefit from such studies and this is reflected in his book.

In this lies much of its value both to the service medical officer and the civilian practitioner.

To the British and to most American medical officers the subject of tropical medicine is a new one, and to a sound general training must be added contact with tropical diseases and a practical textbook such as this written in the field.

To the Indian medical officer and practitioner in addition to being the work of one of their distinguished teachers this book is valuable in that it reflects as has been said the changes that have occurred in disease during the war.

Space does not allow more than a brief reference to particular subjects, but the attention of the reader is drawn to Dr. Napier's lucid handling of malaria and to the chapter upon kala-azar upon which subject he is the acknowledged authority. Dr. John Lowe has collaborated in many ways, as the author has generously acknowledged, but in particular by his chapter upon leprosy which is a model of clear exposition by a master of the subject.

Dr. Napier explains in his preface that the present volume comprises some two-thirds of the whole. This volume discusses most of the important tropical diseases and is largely complete in itself.

The second volume which should appear this year will contain chapters on yaws, tropical ulcerative conditions, helminthic infections, diet and dietetic diseases, snakes and snake-bite, anemias of the tropics, etc., and an index to the whole.

The present volume may be obtained in a good but temporary binding and when the second volume appears, both may be bound in one volume.

A final word: such diseases as smallpox, enteric fever and fungus diseases, though not strictly tropical diseases, are rare in Britain and the two former are rare in the United States. They are common in the tropics and among the troops, yet they seldom appear in textbooks of tropical medicine. The reviewer suggests that the second edition of the book would be enhanced in value by the inclusion of articles upon these subjects.

C. S.

**RECENT ADVANCES IN MEDICINE: CLINICAL, LABORATORY, THERAPEUTIC.**—By G. E. Beaumont, M.A., D.M. (Oxon.), F.R.C.P., D.P.H. (Lond.), and E. C. Dodds, M.V.O., D.Sc., Ph.D., M.D., F.R.C.P., F.I.C., F.R.S. (Edin.), F.R.S. Eleventh Edition. 1943. J. and A. Churchill Limited, London. Pp. xii plus 412. Illustrated. Price, 18s.

This book which first appeared in 1924 is now in its eleventh edition. As all the other books in this series, the new edition involves re-writing much of the old matter, the incorporation of much new matter and the elimination of 'advances' which are no longer 'recent'. The points of this edition are best explained in the preface:

'In preparing this edition the wartime restrictions as regards paper have necessitated our keeping strictly within our former limits, and so, as nearly a quarter of this volume is fresh material, certain familiar sections of previous editions can no longer be included.'

'The sulphonamide and vitamin chapters have been expanded and brought up to date, and a note written on penicillin. Additions to the kidney chapter include descriptions of the specific gravity and inulin clearance tests of renal function, the compression syndrome, and the dangers associated with the use of mercurial diuretics. The insulin and the dextrose insulin tolerance tests are described in chapter IV, and the varieties of spontaneous hypoglycemia and their treatment are discussed. The account of the liver function tests has been largely re-written, and the value of the more recent methods is assessed. Additional notes have been made on the treatment of hæmatemesis, and the use of the continuous intragastric drip for certain types of peptic ulcer is considered. The sex hormone chapter has been partly re-written. Fresh articles include the circulation time, blast injuries of the lungs, "acid" phosphatase, plasma protein regeneration and amino-acid therapy, the blood groups, the Rh

factor, the hazards of blood transfusion, and thymectomy in myasthenia gravis. In the last chapter the photoelectric colorimeter is described, and methods are given for the estimation of sulphonamide drugs in blood and urine. New methods are described for the determination of the icterus index and for the estimation of hæmoglobin. Two new figures are inserted.

The 14 chapters of this book now cover the sulphonamides and penicillin, the vitamins, the kidneys, glycosuria and diabetes, hepatic function, the stomach, the treatment of Addison's disease, the cardiovascular system, the lungs, the sex hormones, the immunology of diphtheria and the treatment of carriers, the nervous system, the hæmopoietic system and blood and urine analysis. A very useful book.

J. L.

**TEXTBOOK OF MIDWIFERY.**—By Wilfred Shaw, M.A., M.D. (Cantab.), F.R.C.S. (Eng.), F.R.C.O.G. 1943. J. and A. Churchill Limited, London. Pp. xiii plus 588, with 246 illustrations. Price, 21s.

THIS is a new work by this well-known teacher of the subject; the author's textbook of gynaecology is well known.

In a preface, the author outlines his attitude to the subject of midwifery; this preface is purposely written in a provocative style and attempts to combine wit and wisdom. This preface may amuse and interest some readers; most readers will think that it is not a valuable part of the book. Very few medical men can make a success of this sort of thing, and the author is apparently not one of them.

The book is along fairly conventional lines, except in a few matters; some technical points may be open to criticism. It is extraordinary in a book dated 1943 to find no mention even of the Rh factor.

A useful book but no great advance on other similar books.

## Correspondence

### THE STATUS OF PHYSIOLOGY

SIR,—All those who have the interest of physiology at heart and wish to see its status raised as an independent science would be glad to read a message from Professor A. V. Hill, F.R.S., which he sent at my request in 1937. I read it out to the Section of Physiology at the 24th Session of the Indian Science Congress which was held at Hyderabad (Deccan) at that time. Now that Professor Hill has happily been amongst us for some months, I take this opportunity to reproduce the message with his permission.

'If Science had no other purpose at all, no other result, it would probably be worth while for ordinary people to encourage it because of its international quality. Collaboration between different groups, different countries, and different races seems to be far easier in scientific matters than in any others: perhaps because there is a court of appeal, *viz.* Nature, which will settle disputes by experiment, and opinion and emotion are not the only guides. I am often astonished when I realize how far my only circle of friends and collaborators is international. It never occurs to one that they are of a different race or nation. They are just citizens of the scientific community.

'India is well on the way. In some subjects, particularly in physics and mathematics, Indians are already collaborating very effectively with the rest of the world. Indian scientists are beginning to be known, in person and by their work, in all the countries of the world. You must see that this becomes true also of physiology. How to do it I cannot tell you—I do not know your conditions well enough. Somehow you must make physiology 'intellectually respectable', so that men of really first-class ability will be attracted to it. At Cambridge, as you know, physiology is just as

'respectable' as physics: it is certainly just as difficult as physics. Claim for it an independent and honourable place such as physics has: do not let it be just a handmaiden (as the old saying was) of medicine. Physics is not the handmaiden of engineering. If it had been, engineering would be in a bad way, for modern engineering depends upon physical knowledge and physics would have made no progress if it had been the handmaiden of any other science or art. Independence and an honourable position are required, and if you can help to give physiology in India these, you will get first-class youngsters in to join it. A danger is that no man may be allowed to hold any place of importance in physiology unless he has a medical degree. Avoid this tradition like poison. It means that you will miss many of the ablest people of all your Pasteurs, Langleys, Barcrofts, Cannons, Baylisses, Howells, Bronks, Lucases, Mineses, Kroughs, Lapicques. We shall look forward in England to seeing your able young men working with us: be sure that they are able before you send them, or they will waste their time and ours. Lim, the Chinese physiologist, asked me if I would have a pupil of his to work with me. I said "yes, if you can send me a really good one. It's a waste of time otherwise". He sent me his best, T. P. Feng, who is so good that I put him as high as anyone I have ever had (and that is pretty good). It is quality, not quantity or numbers, which counts in physiology. All men are not equal—one Rutherford is worth 100 ordinary physicists, one Pavlov produced more effect than 10,000,000 ordinary Russians in winning respect for his country. So guard and watch for and nurse the able youngster, and make things easy for him, and let him have as much independence as he can bear; and then send him out to see how things are done here or elsewhere. He will make friends, he will win respect for his ability, he will aid in establishing in India also that international brotherhood which is superior to race, religion, politics, disturbances, even to scientific differences of opinion—the international brotherhood of scientific people'.

These inspiring words are addressed to all physiologists, medical men and scientists in India, and they are as true to-day as they were in 1937. Professor Hill tells me that, in the meantime, he has not changed his mind in the least.

Needless to say, physiology is of inestimable value in dealing with many problems—social problems such as those of inheritance, eugenics and the population problem, nutrition and physical well-being of the race. It should not merely remain as hitherto as a part of the medical curriculum but should be treated in its own right as an independent science like physics and chemistry. It is only then that physiology would make rapid progress in this country. We must do all we can to create suitable conditions for its healthy growth in our colleges and universities. It must attract the very best men to its service, the best of students and the best of teachers.

S. L. BHATIA, M.C., M.A., M.D. (Cantab.),  
F.R.C.P. (Lond.), F.R.S.(E.),

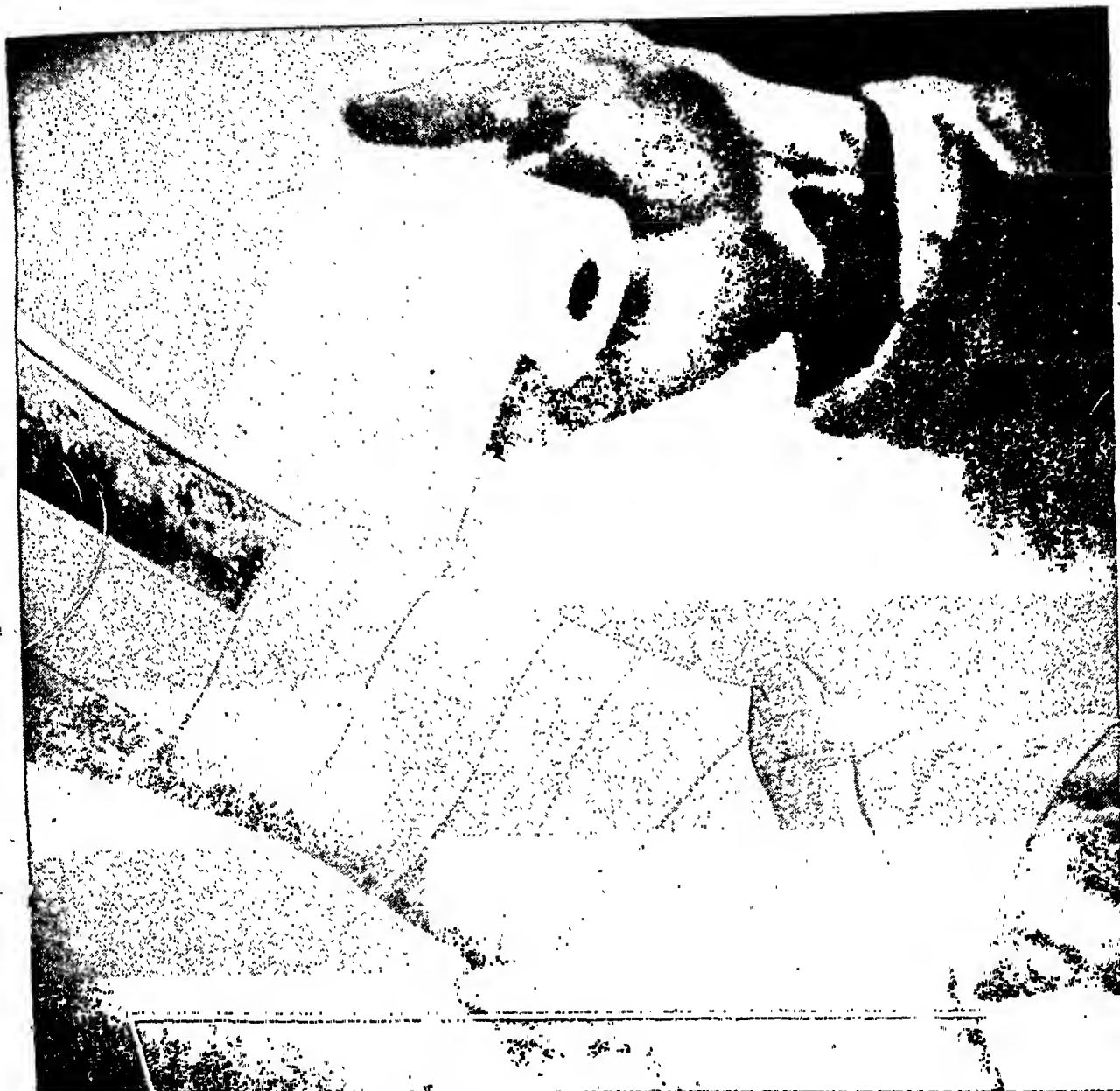
NEW DELHI.  
3rd April, 1944. COLONEL, I.M.S.  
Deputy Director-General, Indian Medical Service.

### HUMERO-SCAPULAR PERIARTHRITIS\*

SIR,—I was very much interested in the article, 'Humero-Scapular Periarthritis' by Dozent Dr. Georg Politzer, in the March issue of the *Indian Medical Gazette*. I have myself published an account of the same disease in the January 1943 issue of the *Antiseptic*. I was not then aware of any literature published on this subject in India or elsewhere. I have seen scores of cases during my practice of twenty-two years and followed them for years. It was always a problem to

\* Rearranged by the Editor.





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me why this type of arthritis should affect the shoulder only and why any specific treatment should have no curative effect on the disease. After a lapse of some months the complaint does pass away without relapse or recurrence in any other joint. Restriction of movements together with pain over the head of the humerus extending down the arm which has to be kept in an adducted position, the age of the patient which is always above 40, no involvement of any other joint and ultimate recovery after some months are all points which make up a disease entity but it has not received the attention it deserves from the medical profession. Dr. Politzer in his article has given a very good anatomical and pathological account which explains the specific features of the disease. The disease is chronic and is likely to pass unnoticed unless patients are followed for some years.

P. S. GUPTE, M.B., B.S.

NASIK (G. I. P. RLX.),  
24th April, 1944.

### BACTERIUM ALCALIGENES INFECTION

SIR,—Dr. R. N. Chaudhuri published case notes of *Bacterium alcaligenes* infection resembling typhoid fever in the April issue of your journal. That some of the cases of typhoid-like fever may be of this origin had been described by previous workers also. I described similar cases either of primary origin or succeeding typhoid fever (resembling a relapse) in the *Indian Journal of Medicine*, Vol. X, 1929, p. 207: in these cases blood culture was positive. Those that resembled typhoid relapse were probably cases of entry of the organisms into the general circulation through the intestinal ulcers. Bacteriologically undiagnosed tropical fevers are yet in such a number that we welcome this report of Dr. Chaudhuri in reiterating the need for thorough investigation of all cases by every possible means and enrich the Indian medical literature with accurate scientific information.

A. R. MAJUMDER,  
Superintendent.

CAMPBELL MEDICAL SCHOOL  
AND HOSPITAL,  
CALCUTTA,  
20th May, 1944.

## Service Notes

### APPOINTMENTS AND TRANSFERS

COLONEL T. C. BOYD, I.M.S. (Retd.), is appointed Additional Deputy Director-General, Indian Medical Service (Personnel), with effect from the afternoon of the 29th December, 1943.

Lieutenant-Colonel C. A. Bozman is appointed Additional Public Health Commissioner with the Government of India, with effect from the 30th December, 1943.

Lieutenant-Colonel L. K. Ledger, O.B.E., is appointed as Residency Surgeon, Hyderabad, with effect from the afternoon of the 17th March, 1944.

Lieutenant-Colonel S. L. Patney is appointed to act as the Inspector-General of Prisons, Bengal, during the absence, on leave, of Lieutenant-Colonel M. A. Singh, or until further orders, with effect from the 24th May, 1944.

On arrival in Bengal, after the expiry of his leave, Lieutenant-Colonel R. A. Wesson is appointed as Civil Surgeon, Faridpur, *vice* Dr. G. C. Sarkar.

Lieutenant-Colonel Das, M.C., is appointed to act as wholetime Superintendent and Medical Officer of the Alipore Central Jail, with effect from the date on which he takes over charge of the jail, *vice* Mr. H. W. Shea and Dr. Bankim Behari Roy.

Captain R. K. Garde, I.M.S. (E.C.), Additional Officer, Medical Store Depot, Calcutta, is transferred as Additional Officer to Medical Store Depot, Bombay, with effect from 25th April, 1944.

LAND FORCES  
SECONDED TO INDIAN ARMY MEDICAL CORPS

To be Captain

Terence Brady. Dated 23rd March, 1943.

INDIAN LAND FORCES  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

To be Captains

3rd April, 1943

Khogendra Nath Ghosh.

Narayana Pillay Madhavan Nair.

Mohammad Shah Nawaz Khan.

Maganlal Premchand Vora. Dated 4th February, 1944.

12th February, 1944

Govind Anant Bhagwat.

Ankes Kumar Chakrabarti.

Anjur Subramania Ramachandran. Dated 18th February, 1944.

Prakas Chandra Sen. Dated 14th March, 1944.

(Miss) Lourda D'Cunha. Dated 17th January, 1944.

Pudur Doraiswamy. Dated 20th February, 1944.

Newa Lal Jha. Dated 18th March, 1944.

Vilas Sakhamam Paranjpe. Dated 19th March, 1944.

Chandrakant Narayan Pradhan. Dated 21st March, 1944.

Meherji Phiroze Mehta. Dated 29th February, 1944.

Pritam Das. Dated 22nd February, 1944.

INDIAN LAND FORCES  
FOR SERVICE WITH THE ROYAL INDIAN NAVY

(Emergency Commissions)

To be Captain

Raj Narain. Dated 20th March, 1944.

INDIAN LAND FORCES

(Permanent Commission)

To be Captain (on probation)

Amar Nath Roy. Dated 20th March, 1944.

INDIAN LAND FORCES  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commissions)

To be Lieutenants

3rd April, 1943

Kenneth Albert DeRozario.

Ralph Stanley Corbitt.

Poland Carlyle Watson.

William Lawrence McKenzie.

Alfred Backman.

George William Lewis D'Sena. Dated 17th November, 1943.

James Yates. Dated 24th November, 1943.

15th December, 1943

Douglas Hammond Niblett.

Terance Albert D'Sena.

Roland Mervyn Stanley Terry.

Ivan Joseph Paul Woodhouse. Dated 5th February, 1944.

Joseph Anthony Righton. Dated 18th February, 1944.

24th March, 1944

George Crosse.

Gerald Francis Perry.

To be Lieutenants

M. Dakshina Murthy. Dated 15th January, 1944.

(Miss) Khurshid-un-Nissa Chaudri. Dated 7th February, 1944.

20th February, 1944

Kshitindra Nath Sen Gupta. Dibakar Kundu.  
Iqbal Mohd. Chaudhri. Dated 1st March, 1944.  
Satya Pal Verma. Dated 13th March, 1944.

14th March, 1944

Joseph George. S. M. Jaffar.  
Sahibzada Mohd. Hashim. Dated 15th March, 1944.

22nd January, 1944

Sudhansu Kumar Mitra. Santosh Kumar Sen.  
Pejavar Vankat Rao. Dated 13th February, 1944.  
Bodapati Ramanarayanamurty. Dated 15th February, 1944.  
Nadimpalli Naga Bhushanam. Dated 18th February, 1944.  
Harold Thakurdas. Dated 1st March, 1944.  
Denzil Horatio Waller. Dated 4th November, 1943.  
(Miss) Sarah Chaekalamanni Thomas. Dated 20th February, 1944.

## LEAVE

Lieutenant-Colonel J. C. Drummond, Surgeon-Superintendent, Presidency General Hospital, Calcutta, is granted leave on average pay for 6 months, with effect from the 19th March, 1944.

Modification of previous orders Lieutenant-Colonel M. A. Singh, Inspector-General of Prisons, Bengal, is allowed leave on average pay for 4 months, with effect from the 9th May, 1944.

## PROMOTIONS

Major to be Lieutenant-Colonel

A. N. Chopra. Dated 17th April, 1944.

Captains to be Majors

W. Fleming. Dated 22nd November, 1942.

23rd April, 1944

M. G. Leane. D. P. Dewe.  
G. E. S. Stewart, M.B.E. I. J. Franklen-Evans.  
V. D'A. Blackburn. Dated 11th April, 1944.

## INDIAN LAND FORCES

SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commission)

Captain to be Major

V. Sivasankaran. Dated 19th March, 1944.

The undermentioned officer is granted the local rank of Major without effect on pay and pension, whilst employed as a Senior Recruiting Medical Officer :—  
Captain S. R. Sethi, I.M.S./I.A.M.C. Dated 14th September, 1943.

Lieutenants to be Captains

3rd April, 1944

K. A. DeRózario. R. C. Watson.  
R. S. Corbitt. W. L. McKenzie.

A. Backman.

O. H. Drake. Dated 18th August, 1943.  
G. T. Wallace. Dated 17th September, 1943.  
M. K. Hashmi. Dated 1st March, 1944.

2nd April, 1944

P. J. Fernandes. W. B. A. D'Souza.  
F. W. Ferreira. Dated 4th April, 1944.

6th April, 1944

K. G. V. Bhagavan Narayan. A. J. Nicholas.

7th April, 1944

C. J. Pereira. G. A. Burby.

E. L. C. Pushong.

K. C. Banerjee. Dated 8th April, 1944.

E. M. Wilson. Dated 9th April, 1944.

D. C. Wilkins. Dated 10th April, 1944.

13th April, 1944

C. M. Hogg. C. J. Hart.

S. R. E. Kitto. Dated 17th April, 1944.

B. G. Bamford. Dated 19th April, 1944.

R. P. Harvey. Dated 21st April, 1944.

P. R. Ramachandrudu. Dated 22nd April, 1944.

R. Ganguly. Dated 29th April, 1944.

30th April, 1944.

R. Narayanan.

A. J. Arunagiri.

T. S. Ramaratnam.

C. R. Suryanarayan.

G. K. Atluri.

P. V. Krishnamurti.

B. V. Rama Rao.

## INDIAN LAND FORCES

(Emergency Commissions)

(SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY)

Licutenant to be Captain

B. S. Moos. Dated 20th April, 1944.

(Emergency Commissions)

(WOMEN'S BRANCH)

Lieutenants to be Captains

(Miss) D. E. Thomas. Dated 28th February, 1944.

(Miss) M. S. Sheikh. Dated 24th March, 1944.

(Miss) N. D. Chadda. Dated 4th April, 1944.

(Miss) S. Aziz. Dated 18th April, 1944.

(Miss) R. A. Gulmohamed. Dated 20th April, 1944.

(Miss) K. S. Jaya Lakshmi. Dated 26th April, 1944.

## RETIREMENTS

Colonel H. E. Shortt, C.I.E. Dated 15th April, 1944.

Lieutenant-Colonel D. R. Thomas, O.B.E. Dated 12th April, 1944.

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## Original Articles

LIVER FUNCTION IN AMOEBIASIS  
AND ITS VARIATIONS UNDER  
EMETINE THERAPY

By ROBERT HEILIG, M.D.

First Physician, Krishnarajendra Hospital and Professor  
of Medicine, Medical College, Mysore

and

S. K. VISVESWAR, M.B., B.S.

Research Assistant, Krishnarajendra Hospital, Mysore

THE question whether amoebic dysentery influences the liver function arose from the experience that a definite discrepancy exists between the fact, fully established, that *Entamoeba histolytica* does not produce a toxin, and the clinical impression that patients suffering from acute or chronic intestinal amoebiasis look and behave as if they were 'toxic'; moreover, anorexia, emaciation, sallow complexion, hyper-irritability or a neurasthenic mentality, developing in cases of chronic amoebic dysentery (without clinical hepatitis) and quickly disappearing under emetine therapy, remind so much of the symptoms characteristic of hepatic deficiency; that an investigation of the liver function, prior to and following the administration of emetine, seemed justified. Estimations of the liver efficiency in amoebic hepatitis have been performed because of the scarcity of data available in literature and textbooks pertaining to this question. It was a logical consequence of the foregoing considerations to find out whether clinical improvement of the local and general condition in hepatic amoebiasis, under the influence of emetine therapy, is accompanied by any consistent variations of the liver function.

## Method of investigation

Fifteen patients with acute or subacute amoebic dysentery, many of whom gave a history of previous similar attacks, and eleven patients with acute amoebic hepatitis have been selected; they were free from hookworm disease and active signs of malaria. It was not possible completely to exclude urinary tract infections, almost every diarrhoea leading sooner or later to an involvement of the urinary tract (Leishman, 1939; Heilig and Puttaiya, 1943). The diagnosis of amoebic dysentery was established by microscopic examination of the faeces, and that of amoebic hepatitis by the history of dysentery in the past, by the presence of an extremely tender liver, enlarged on palpation and on radiological examination, of fever and leucocytosis, and of rapid response to emetine treatment. A liver-function test was performed on admission (i.e. before emetine medication) after six emetine injections (1 grain each) and after twelve doses of emetine which brought the total dosage to 12 grains.

For estimating the liver efficiency, the original Quick's hippuric-acid test (Quick, 1931) was used, which is generally recognized as one of the most reliable liver-function tests. We preferred the oral method, the intravenous modifications being too sensitive and sometimes yielding pathological results in conditions of a functional impairment which is too slight to be of clinical significance.

The mode of procedure was that the patients received milk and bread at 7 a.m. One hour later the patient was made to empty his bladder, this urine being discarded; now 6 gm. of sodium benzoate was given, well dissolved in about 50 c.cm. of water, followed by 100 c.cm. of water taken from the same vessel, to ascertain that the whole amount of benzoate was ingested. For the next 4 hours the patient was not allowed to take food or water, and was kept in bed. All the urine passed within these 4 hours was collected in hourly samples, which were pooled by the end of the test and divided into two equal parts, in both of which, parallel estimations of hippuric acid were performed. Hereafter, the urine was acidified with 1 to 2 c.cm. of dilute acetic acid, and concentrated on an electric boiling water-bath until the final volume was reduced to 20 to 25 c.cm. This concentrate was cooled and 1 to 2 c.cm. of concentrated hydrochloric acid was added, sufficient to give a blue colour to congo-red paper. Hippuric acid was allowed to crystallize out at laboratory temperature. The crystalline sediment was collected on a fluted filter-paper and washed frequently with small quantities of cold water. The total volume of the filtrate was measured in order to apply the solubility correction of 0.33 grammes per 100 c.cm. of the filtrate at 25°C. to 26°C. The hippuric acid was dried and weighed to constant weight. To express the results in terms of benzoic acid, the figure for the weight of hippuric acid obtained was multiplied by 0.68.

According to Quick, a normal adult excretes 3 grammes of benzoic acid in the form of hippuric acid in 4 hours, the normal range varying between 80 and 120 per cent of this amount. The results are tabulated below.

## Results

Considering the figures obtained in amoebic dysentery cases before emetine treatment, we find 7 out of 15 showing a moderate or considerable impairment of the liver function, which in the average of this group amounts to 55.4 per cent. After the administration of 6 grains of emetine, the liver efficiency of only 3 cases (out of 14) is below the lowest limit of the normal, the average increasing to 72.6; by the end of the course, 1 case (out of 12) shows a definite pathological function and the average of the efficiency rises to 80.2 per cent.

Table II shows that, on admission, 1 case of hepatitis out of 11 showed a definitely damaged liver function, and 2 ranged low, being just within normal limits; after having received 6 and 12 grains of emetine, respectively, all cases responded normally to Quick's test. The average values rose from 69.8 per cent in untreated patients, to 83 after six and 90.4 after twelve emetine injections. Clinically, all these showed a satisfactory improvement.

The blood pressure of the dysentery group and that of the hepatitis group reacted to

TABLE I  
*Liver function in amœbic dysentery*

Age, Sex	Before emetine		After 6 grain      12 grain of emetine				Route of emetine administration	REMARKS
	Liver function in per cent of normal	Blood pressure mm. Hg.	Liver function in per cent of normal	Blood pressure mm. Hg.	Liver function in per cent of normal	Blood pressure mm. Hg.		
(1) 16, M.	78	92/64	89	85/60	99	82/56	Intravenous	Moderate dysentery.
(2) 16, M.	48	88/60	75	82/58	98	80/58	"	" "
(3) 36, M.	42	100/64	58	95/60	..	92/58	"	" "
(4) 15, F.	59	120/80	47	100/72	38	95/70	Intramuscular	" "
(5) 35, F.	57	105/85	91	..	..	98/80	"	Did not co-operate.
(6) 40, F.	32	110/60	..	102/60	97	105/65	Intravenous	Severe dysentery.
(7) 65, M.	40	100/60	45	..	58	95/58	"	Moderate dysentery.
(8) 40, F.	27	..	32	..	51	..	"	"
(9) 32, M.	83	115/75	94	103/72	..	105/75	"	Severe dysentery.
(10) 38, M.	86	85/55	93	100/65	107	100/65	"	" "
(11) 17, F.	22	140/80	60	130/80	66	110/80	Intramuscular	Mild dysentery.
(12) 53, M.	76	100/66	84	84/56	88	88/64	Intravenous	Moderate dysentery.
(13) 25, M.	42	95/48	80	98/48	83	98/50	"	"
(14) 35, M.	65	115/85	88	100/80	86	100/80	Intramuscular	Severe dysentery.
(15) 21, M.	74	118/60	83	..	92	110/62	"	" "
Average of liver function	55.4		72.6		80.2			

TABLE II  
*Liver function in amœbic hepatitis*

Age, Sex	Before emetine		After 6 grain      12 grain of emetine				Route of emetine administration.
	Liver func- tion in per cent of normal	Blood pressure mm. Hg.	Liver func- tion in per cent of normal	Blood pressure mm. Hg.	Liver func- tion in per cent of normal	Blood pressure mm. Hg.	
(1) 45, M.	38	..	66	..	86	..	Intramuscular.
(2) 32, M.	88	110/70	..	100/65	99	98/65	"
(3) 46, M.	65	132/90	..	..	97	120/85	"
(4) 35, M.	..	..	86	..	72	..	"
(5) 22, M.	71	120/80	93	104/60	101	100/62	Intravenous.
(6) 40, M.	66	105/75	77	98/70	78	100/72	Intramuscular.
(7) 30, M.	80	110/60	87	100/60	93	100/65	Intravenous.
(8) 30, M.	96	100/55	97	98/58	105	98/55	"
(9) 18, F.	54	110/70	82	110/75	90	90/58	Intramuscular.
(10) 48, M.	55	100/68	62	98/70	74	95/58	Intravenous.
(11) 30, M.	85	100/65	96	98/70	99	98/68	"
Average of liver function	69.8		83		90.4		

emetine in much the same way, making a separate consideration unnecessary. The ortho-diagrams, partly considered in a previous paper (Heilig and Visveswar, 1943), showed no significant changes under the influence of emetine or the condition for which the patients have been treated.

#### Discussion

Quick's hippuric-acid test estimates two partial functions of the liver: its capacity of glycine synthesis and the enzymatic power of conjugating glycine with benzoic acid to hippuric acid. If insufficient glycine is produced, or if the enzymatic function of coupling is impaired, the

amount of hippuric acid excreted in the urine is diminished. The advantage of checking by one test two physiological functions of the liver recommends this method for clinical use; moreover it is a simple and accurate gravimetric method; though not as sensitive as the intravenous modification (Quick, *et al.*, 1938), it is sufficiently sensitive to indicate all hepatic functional disorders which are of clinical significance. Apart from Quick's (1931, 1933, 1935, 1936) numerous investigations, the reliability of this test was confirmed by Snell (1935), Snell and Magath (1938), Probst and Londe (1940), Heilig and Kantiengar (1942), Mateer *et al.* (1943) and many others. The results are not appreciably affected by disorders of other organs; a renal retention of hippuric acid takes place only parallel with a considerable nitrogen retention (Snapper and Grünbaum, 1924). It seems, therefore, that the introduction of the hippuric acid test constitutes a definite advance over the previously employed methods; of these Mann (1934) said that, in dogs, almost the whole liver could be removed without yielding pathological results when these tests were used.

It is surprising that textbooks of tropical medicine make no mention at all of the liver function in amoebic dysentery. On perusing the Quarterly Cumulative Index Medicus from 1931 to 1943 we found one Italian and one German paper pertaining to this subject. The former (Cordaro, 1938) is not available to us. The latter (Gminder, 1939) reports results from the Gold Coast, obtained by performing the Takata-Ara test in 9 cases of acute and 14 cases of chronic amoebic dysentery. Whereas in the former group the reaction was negative, the chronic dysenteries showed some indication of a parenchymatous liver damage in 10 cases; in 3 of them the impairment was considerable. The influence of emetine on these findings was not investigated.

It is to be expected that in a country such as India where so many toxic factors are constantly in operation which diminish the liver efficiency, the lower limit of normal function should be far below that which was found by Quick in the U.S.A. In fact, in an investigation, performed on healthy medical girl students in Mysore (Heilig and Kantiengar, *loc. cit.*), the efficiency figures (in the menstrual period) varied between 56 and 117 per cent, being diminished during menstruation up to 28 per cent in one apparently healthy individual. In accordance with this experience, which shows an interesting parallelism to the low urea clearance values found in normal Indians (Gokhale, 1941), we fixed tentatively 55 per cent as the lowest limit of a normal liver function.

Seven out of 15 dysentery cases included in this series fall short even of this limit, and the average efficiency, 55.4 per cent, is just on the border line of physiological function. These facts show that a considerable amount of toxin is absorbed into the portal circulation during

the course of amoebic dysentery. There is no doubt that these toxins are not produced by the amoebæ; but the latter act as pace-makers for the bacterial flora and its toxic products, which are able to exert their damaging effect on the liver, due to the break-down of the barrier function which is vested in the normal intestinal mucosa. The importance of accompanying bacterial toxins in the development of amoebic lesions in the liver of cats was pointed out by Cleveland and Collier (1930) and Cleveland and Sanders (1930); the fact that *E. histolytica*, living in the human intestines, may not cause any pathological signs unless pathogenic bacteria are present too, was established by Westphal in experiments on himself and on a colleague serving as control. Craig (1940) ascribed the toxic symptoms of non-dysenteric amoeba carriers exclusively to the action of the bacteria. On the other hand, Comfort *et al.* (1938) found hepatic insufficiency in 4 cases of ulcerative colitis, which supports our view that the liver damage found in almost 50 per cent of amoebic dysentery cases is due to toxin absorption from the ulcerated surface of the colon. It is noteworthy in this connection that only one of our dysentery patients (no. 5) showed a slight tenderness and enlargement of the liver and a leucocyte count of 18,000, thus making a hepatitis probable; but this case had a liver efficiency (57 per cent) within normal limits. Another factor which could be responsible for the liver damage in dysentery is dehydration and loss of sodium chloride; Mason and Lemon (1932) and Collier *et al.* (1936) found the former, and Collier *et al.* (1938) the latter, responsible for functional impairment in hepatic conditions. In the present series, the low value of 27 in case 8 could partly be due to these concomitant factors, whereas in the worst case of all (case 11), showing an efficiency of only 22 per cent, the number of motions did not exceed five per day; in case 6, with 32 per cent efficiency, four or five motions a day were being passed on admission; of course, it is possible that on the previous days the number of motions was greater, causing a considerable reduction of the fluid and salt content of the tissues, although the clinical appearance of these patients did not support such an assumption. Anæmia which is widely prevalent among our hospital patients, apparently, does not much influence the results of the Quick's test. Fouts *et al.* (1937) obtained normal values, with an average of 86.3 per cent, in 45 cases of pernicious anæmia.

The excellent effect of emetine, 6 grains of which increased the average efficiency from 55.4 to 72.6, and 12 grains to 80.2, could easily be explained by its healing effect on the amoebic ulcers; one single cell layer of sound granulation tissue covering the floor of the ulcerations prevents further toxin absorption, thus giving a chance to the regenerative powers of the liver to repair the damage. Apart from the specific effect on *E. histolytica*, emetine, due to its



protoplasmic toxicité, acts as a general intestinal disinfectant, preventing the further production of bacterial toxins by inhibiting bacterial growth. Although this unspecific emetine effect is desirable in amœbic dysentery, it would be a serious mistake to make use of it in non-amœbic intestinal infections, which could be cured by far less toxic drugs or even without drugs.

The assumption that bacterial toxins are responsible for the functional liver damage found in amœbic dysentery is in accord with the experience that such toxins substantially contribute to the development of cirrhosis in experimental animals (Moon, 1932, 1934, cf. Boyd, 1940) and conforms well to the opinion, expressed by Megaw (Manson-Bahr, 1940) and Gibbons (Manson-Bahr, 1940), that infantile biliary cirrhosis is caused by intestinal toxins (bacillary dysentery or a toxin of gastric origin). Our findings also provide a firmer base for the theory that the frequent occurrence of portal cirrhosis in South India, the Dutch East Indies, etc., appearing independently of alcohol consumption and syphilis, is due to the absorption of toxins from the large intestines in chronic bacillary or in amœbic dysentery (Strong, 1942). The close connection between intestinal amœbiasis and impairment of the liver efficiency, restoration of which is so easily achieved by properly administered emetine treatment, emphasizes the importance and urgency of making the right diagnosis, especially in recurrent intestinal disturbances.

A further, almost definite, proof that not the amœbic but the accompanying bacterial infection interferes with the hippuric-acid synthesis in many cases of amœbic dysentery is to be found in the fact that amœbic hepatitis affects the liver functions much less. Previous investigations of the liver function in this condition, performed for diagnostic purposes, 'have frequently proved unsatisfactory' (Strong, *loc. cit.*). Brown and Hodgson (1938), using the bromsulphalein test, found indications of liver damage in 8 out of 13 cases. In the literature at our disposal, we found only a few estimations of liver efficiency in amœbic hepatitis performed with Quick's test, though this method was frequently used in other forms of hepatitis. Probstein and Londe (*loc. cit.*), using a modification of Quick's technique (Weichselbaum and Probstein, 1939) which yields somewhat higher normal values, found an efficiency of 53 to 72 per cent in 3 cases of arsenic hepatitis; in 18 cases of various hepatic diseases, these authors obtained the lowest value of 26 per cent in liver cirrhosis, the highest of 89 in a cirrhosis-like condition characterized by repeated gastric hæmorrhages. Boyce (1941), who applied the original method of Quick, reported 50.5 per cent in 1 fatal case of amœbic abscess, 23.06 to 97.6 in 7 cases of toxic hepatitis and 70.5 to 72.3 per cent in 2 cases of cirrhosis.

Our results confirm the view that liver-function tests rarely help in establishing an early diagnosis

of amœbic hepatic involvement. Using Indian standards, only 1 of our 10 cases showed considerable liver damage, and 2 more yielded results on the lowest limit of physiological function, the average value of efficiency (69.8 per cent) being well within the normal range. Applying American standards, 6 of 11 cases would fall into the range of pathological function, a proportion equal to that which has been found by Brown and Hodgson (*loc. cit.*).

To establish definitely physiological standard values for India, function tests in normal individuals have to be performed on a much larger scale than we did (Heilig and Kantiengar, *loc. cit.*). However, comparing the results obtained in amœbic dysentery with those of hepatitis, the conclusion seems to be justified that in the latter condition, toxic lesions are less often to be found and less extensive than in the former. This result is not surprising. The contents of an amœbic abscess are usually sterile, bacterial toxins thus being absent; moreover a diffuse, though not necessarily severe, liver cell damage is necessary to produce clinical proofs of a considerably impaired function, whereas amœbic lesions are confined to the site of the amœbæ, no diffusible toxin being produced by them. The liver tissue, not being damaged by the direct action of the proteolytic enzyme (to which the *entamoeba* owes its name *histolytica*), remains morphologically and functionally intact, just as the intervening colonic mucosa between the ulcers is healthy.

In spite of the rarity of a severe hepatic insufficiency in our small series of cases of hepatitis, serial function tests performed during and after emetine treatment revealed that some functional impairment was present in almost every case; all but one showed a definite improvement following emetine administration. The average value of 69.8 before treatment rose to 83 after 6 and to 90.4 per cent after 12 grains of emetine.

The beneficial effect of therapeutic emetine doses on the liver function should not tempt anybody to use emetine in hepatic diseases which are not of amœbic origin. In toxic doses, emetine is a liver poison which in rabbits causes congestion and fatty degeneration (Chopra *et al.*, 1924) or focal necrosis (Rinehart and Anderson, 1931).

### Conclusion

The results of liver-function tests performed with Quick's hippuric-acid test make it probable that the liver efficiency is diminished in about one half of amœbic dysentery cases. The damaging agents are supposed to be bacterial toxins absorbed from the intestinal mucosa, a conclusion which is supported by the fact that emetine medication brings about a prompt and considerable improvement of the liver function.

In patients suffering from amœbic hepatitis, the frequency and intensity of hepatic impairment tested by the same method is much less.

The absence of diffusible toxins and the circumscribed character of amœbic lesions explain these findings. Emetine, however, increases the liver efficiency in hepatitis, a result which demonstrates the existence of latent lesions even in these cases.

### Summary

In 15 cases of amœbic dysentery and in 11 cases of amœbic hepatitis, the liver function was tested before emetine therapy, after 6 grains and 12 grains of emetine.

The method of investigation used was Quick's hippuric-acid test.

The results have been tabulated and discussed.

An attempt was made to explain the difference between the results obtained in intestinal and those in hepatic amœbiasis.

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## VENTRICULAR TACHYCARDIA OF LONG DURATION (TWENTY DAYS) WITH RECOVERY

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and

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WE have recently had under our care at the King Edward Memorial Hospital, Bombay, a Muslim male, aged 38, with ventricular tachycardia, which continued without intermission for as long as twenty days, and finally terminated in an abrupt manner after a course of intensive quinidine therapy. We have reason to believe that this man had suffered previously (six months prior to this attack) from a similar attack of paroxysmal ventricular tachycardia lasting for over twenty days, which attack had ceased spontaneously without any treatment.

Paroxysmal tachycardia is a fairly common disorder of cardiac rhythm which 'starts suddenly and terminates abruptly' usually within a matter of minutes or hours. The condition of paroxysmal tachycardia was first observed in 1888 by Bristowe and given its present-day designation by Bouveret in 1889.

Three main forms of paroxysmal tachycardia are recognized at the present time, viz, (1) auricular, (2) ventricular, and (3) auriculo-ventricular or nodal. The ventricular form of paroxysmal tachycardia is much less common than the auricular form (ratio of 1:6) and presents a much more serious outlook. Paroxysmal ventricular tachycardia is, as a rule, a transient disturbance of cardiac rhythm, which terminates spontaneously in a matter of seconds, minutes or hours and seldom lasts for more than a few days; according to Christian (1935) 'their duration is always short, not exceeding a few hours'. Attacks of paroxysmal ventricular tachycardia lasting over a week, though

extremely rare, have been recorded from time to time in medical literature.

In the series of cases of paroxysmal ventricular tachycardia reported by Wolferth and McMillan in 1923, the longest paroxysm reported lasted 11 days. Robinson and Herrmann, in 1921, had reported 4 cases of their own of paroxysmal tachycardia of ventricular origin, in one of which the attack is said to have lasted about 11 days.

Porter's case (1924) had an attack of ventricular tachycardia lasting 153 hours (or approximately 6 days), with recovery; in this case, there was evidence of coronary thrombosis with grave myocardial disease. The electro-cardiogram of this case showed 'dissociated auricular activity' as well as 'unusual alteration of ventricular complexes'.

In 1929, Levine and Fulton reported a fatal case of ventricular tachycardia, in which the paroxysm had continued for as long as 14 days.

In 1932, another fatal attack of paroxysmal ventricular tachycardia, lasting 11 days, was reported by Salley. In this case, quinidine had been tried in large doses from time to time but with partial success only; the rate of the heart had been slowed down repeatedly with quinidine from about 160 or 170 to about 110 per minute, but this effect was quite transitory. After 11 days of quinidine therapy, atropine sulphate was given a trial, 0.002 gm. being injected subcutaneously; within 7 minutes of the injection, the pulse rate fell to 30 per minute and the electro-cardiogram revealed complete heart-block, the ventricles beating at a rate of 30 per minute and the auricles at 98 per minute. It was suggested that atropine might have broken up the circus movement in this case, by its paralysing action on the vagus nerve.

In 1934, Elliott and Fenn reported an unusual case of long-continued ventricular tachycardia, lasting for as long as 32 days and with a fatal termination.

In 1940, Strong and Munroe described an attack of ventricular tachycardia in a man of 41, in which the attack, which had lasted without intermission for 23 days, responded finally, in a dramatic manner, to a massive intravenous injection of 40 grains of quinidine. Their case is probably the longest attack of ventricular tachycardia with recovery on record. An atypical feature, noted in this case, was the gradual reduction in cardiac rate at the termination of the attack. The heart-rate dropped from an initial rate of 176 per minute (at the start of intravenous quinidine injection) to 96 per minute at the end of two hours and prior to the actual resumption of 'sinus rhythm', there was noted, for a short but undeterminate length of time, a 'phase of supraventricular tachycardia'. Another unusual feature noted by Strong and Munroe in this case was the characteristic effect of quinidine on cardiac rate. On several occasions during the course of the paroxysm, the rate of the heart was reduced quite appreciably (without any change in the abnormal rhythm) by the administration, oral and intravenous, of quinidine; this drop in rate amounted to 39 and even 50 beats per minute, on several occasions. Severe toxic symptoms were noted by these authors; after their massive dose of intravenous quinidine they report vomiting, rise of blood pressure, burning all over the body, loss of consciousness, severe generalized epileptiform convulsions, tinnitus, vertigo, and headache. Because of such toxic manifestations, Strong and Munroe suggest restricting the use of intravenous quinidine to grave paroxysms of ventricular tachycardia, and only after a fair trial of oral medication of quinidine.

Mays (1942) has recently reported a case of ventricular tachycardia, which is probably the most striking of all the cases of this condition on record. He described a fatal attack of ventricular tachycardia in a 59-year old Polish cabinet-maker which lasted for as long as 77 days, in spite of medical treatment, and terminated fatally; their patient received in all 22.5 grains of digitalis, several injections of acetyl-beta methylcholine chloride (together with carotid sinus

pressure), one intravenous injection of magnesium sulphate, two intravenous injections of quinine dihydrochloride and three intravenous injections of quinidine sulphate. Post-mortem examination revealed thrombosis of the coronary artery with infarction and involvement of the interventricular septum; there was also a gross dilatation of the left ventricular wall.

The following case-report and clinical description of an attack probably represents the second longest paroxysm of ventricular tachycardia with recovery on record; in our case, the length of the paroxysm was 20 days; the longest paroxysm on record (with survival) has been reported as 23 days by Strong and Munroe (1940).

Another feature of interest in this case is the complete and sharp inversion of the T waves noted in all the leads of the electro-cardiogram immediately after the cessation of the attack and restoration of normal 'sinus rhythm'. Campbell and Elliott (1939) and Campbell (1942) have recently discussed this interesting abnormality of the T wave (sharp inversion of the T wave in one or more leads) occurring soon after long-continued paroxysms of tachycardia. He has given case-reports of five cases of this type, where the T wave inversion was severe enough to suggest the possibility of coronary occlusion. According to him, this T wave inversion does not mean organic disease but is a completely 'reversible process indicating some degree of exhaustion or strain of heart muscle'.

### Case report

A muslim male, aged 38, mill-hand by occupation, was admitted into the King Edward Memorial Hospital, Bombay, on 24th April, 1943, with a 6 days' history of pain in the precordium, 'fluttering sensation in the chest' and persistent vomiting.

These symptoms had come on quite suddenly one day, for no apparent reason, and had persisted ever since, without intermission, until the time of admission. He was unable to retain anything taken by mouth.

He gave a history of a similar attack of 'fluttering' in the past (about six months prior to the present attack), an attack that was said to have lasted without intermission for about 20 days and which had terminated quite suddenly without treatment.

There was a history of joint-pains about 8 or 9 years before admission; no history of syphilis or gonorrhoea. The family history was of no importance.

On examination (24th April, 1943) the patient was found to be very restless and irritable. He was vomiting every few hours and complained of nausea. The nails were not clubbed, the conjunctiva were normal in colour, the neck veins were not engorged and peripheral oedema was absent.

Examination of the cardiovascular system revealed the presence of the apex beat in the fourth space, 5 inches away from middle line. On palpation, a fluttering movement of precordium was detected. The rate of the heart appeared to be regular and too rapid for counting. No thrills were palpable. Percussion confirmed a lateral displacement of the cardiac apex (the lateral margin of the heart being in 4th space, 5 inches from the middle line). On auscultation the heart rate was found to exceed 200 per minute; the exact figure could not be determined. The rhythm appeared to be regular; the two heart sounds were so similar in intensity and character that it was difficult to distinguish one from the other. The rhythm of the sounds was described as 'tic-tac'. Murmurs were not heard in any of the auscultatory areas of the heart. The rhythm of the pulse was regular and there was

no evidence of pulse-deficit. Tension, volume and force of the pulse were recorded as 'poor'. The blood pressure was 104 mm. Hg. systolic and 62 mm. Hg. diastolic.

The liver was found to be tender, being felt two fingers below the costal margin. The spleen was felt on the day of admission, being one finger below the costal margin. There were no signs of free fluid in the abdomen. No abnormalities were detected in any of the other systems.

### Investigations

**Electro-cardiogram.**—The first electro-cardiogram, taken on 27th April (see figure 1, plate XVII), showed a typical picture of ventricular tachycardia, the rate of the ventricular beating being 230 per minute. There was no evidence of any 'dissociation of auricular activity', nor was there any tendency on the part of the rhythm to vary from time to time.

The second electro-cardiogram, taken on 7th May, being no different from the first, is not reproduced here. In spite of digitalis and massive doses of quinidine, the rate of beating was still 230 per minute and quite constant in all the leads.

The third electro-cardiogram (figure 2, plate XVII), taken on 8th May, that is, soon after cessation of the paroxysm, showed restoration of normal sinus rhythm with the heart beating at a rate of 60 per minute. The most striking abnormality at this stage was the complete inversion of the T wave in all the standard leads of the cardiogram. The T wave inversion in this case was not comparable with the T wave inversion associated with the effect of digitalis or with lesions of the coronary arteries. It is possible that the T wave inversion witnessed in this case was of the type described recently by M. Campbell (1939; 1942) as occurring after long paroxysms of tachycardia.

The fourth electro-cardiogram (figure 3, plate XVII), taken on 11th May, shows restoration of the normal upright T wave in at least one lead, lead III, with a tendency towards normal in the other leads.

The fifth electro-cardiogram (figure 4, plate XVII), taken on 15th May, shows a normal T wave on leads II and III and a tendency to return to normal in lead I.

Fluoróscopy during the attack revealed extremely rapid fluttering of the left border of cardiac silhouette. Urine examination showed nothing abnormal while the blood Kahn was negative.

### Treatment

To begin with, the patient was put on large doses of digitalis, 30 minims of standardized tincture being given three times a day. In all, 6½ drachms were administered within first five days in hospital. As the patient failed to show any improvement, the digitalis was stopped. One ampoule of Carbachol was tried intravenously and one ampoule intramuscularly, but with no result.

Quinidine was tried orally (from 28th April, 1943) in doses of 5 grains four-hourly (*i.e.* 30 grains per day) and this was continued for about 10 days. In all, 312 grains of quinidine were administered to this patient during the latter half of the paroxysm. Morphine had to be given for restlessness on several occasions. Ten c.cin. of aminophyllin had also been tried once but with no effect.

### Progress

The patient continued to remain irritable and showed no response to any form of medication until the 7th May (*i.e.* 20 days after the inception of the attack) when his pulse and heart-rate were found to drop from over 200 per minute to 60 per minute. At this time the patient's extremities were found to be cold and clammy. From that time, the heart-rate and pulse have remained normal at about 60 per minute and are quite regular. Although the attack of paroxysmal tachycardia subsided, the patient continued to be restless for a few days more, and was even delirious at times. There has been a slow return to normal within the last few days. It was remarkable that at no time during this attack of 20 days' duration was there any evidence of breathlessness, engorgement of veins, peripheral oedema or congestion of lung bases. A few days after the attack, the heart margins were found to be as during the attack. The apex beat was in the same position, *i.e.*, fourth space 5 inches from middle line. Heart sounds were normal. A soft systolic murmur was heard at mitral area and was not conducted beyond the left border of the heart.

We acknowledge our indebtedness to Dr. A. Hamid, M.D., and to the Dean of the King Edward Memorial Hospital, Bombay, for permission to publish this case.

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## THYMOMA

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TUMOURS of the thymus gland are rare, and the study of these is of importance because of the controversy about their pathology.

Malignant tumours of the thymus are of interest not only on account of their rarity, but also because of the controversy regarding the histogenesis of the gland (Crosby, 1932). Janeway (1920) urged the importance of early diagnosis and familiarity with the clinical course of these tumours, for in a large number of cases radium or x-ray therapy offered relief, even if not a prospect of cure. Roentgen examination is of the utmost diagnostic importance. The location and appearance of the shadow are characteristic.

The pathology of a thymoma is still a matter of controversy and will remain so until histologists agree upon the normal constituents of the thymic parenchyma (Herriman and Rahte, 1929). Foot (1926) observed 'malignant thymomas are distinctly rare, less than a hundred having been described to date. A complete understanding of malignant thymic tumours will, of course, never be arrived at until we know more about the thymus and until the question of the aetiology of malignant tumours in general has been answered. In the meantime, we may assist investigators of both these questions by carefully studying and reporting every case of malignant thymoma'.

In consideration of the above, it has been thought worth while to publish the two cases of thymoma that we have been able to collect since 1900 from the records of the Pathology Department of Calcutta Medical College.

**Case 1.**—S. I., Mohammedan, male, aged 20 years, a fitter by occupation, was admitted in the hospital for—

- (a) Difficulty in breathing—duration, 7 days.
- (b) Swelling of the neck—the same duration.
- (c) Difficulty in swallowing—the same duration.

**History.**—He fell down from a height of 10 feet, having slipped from the steps of a ladder, about two weeks prior to the admission. He felt pain immediately over the chest which gradually subsided. Then the above complaints appeared. X-ray report showed pleuro-mediastinal effusion in the left side and a diagnosis of hæmothorax was made. On aspiration, 20 c.cm. of blood-stained fluid were withdrawn from the left pleural cavity. He died suddenly two days after the aspiration after an acute attack of dyspnoea. The body was sent to the police morgue where, on post mortem, a huge mass was noticed over the cardiac area completely hiding the heart, and it appeared that the mass was composed of thickened pericardium. As a matter of fact the specimen was sent to

us to investigate the nature of the thickened pericardium. On cutting the mass, the heart and pericardium were found to be perfectly normal and completely hidden by the tumour (figure 1, plate XVII).

Histological examination showed the following features:—

The general cell pattern was of small round cell type with a vesicular nucleus; the cytoplasm showed slight acidophilic character. The intracellular substance was very scanty (figure 2, plate XVII). Quite a number of blocks were studied but none showed any Hassall's corpuscles.

**Case 2.**—Sribairi, Hindu, male, aged 10, was admitted on 30th November, 1942, with difficulty in breathing for the last two months, which was gradually getting worse and worse. On examination, marked swellings of the whole of the face and neck, and slight swelling on the anterior chest wall, with engorged superficial veins, were noted. He had a feeble and rapid pulse, 138 per minute, and hurried respiration. He was found to be in acute distress. He died on the same day, and an autopsy was performed.

On opening the chest cavity, a hard nodular mass was seen in the anterior and middle mediastinum. The tumour was seen to infiltrate into the right lung (figure 3, plate XVII). The anterior wall of the pericardium was adherent to the tumour mass, but no infiltration into the pericardium was seen. There was no other significant finding anywhere, nor was there any other focus of metastasis. Histological examination showed the same characteristics as the previous one, *viz.* small lymphocytic type of cells with scanty intracellular substance and absence of Hassall's corpuscles. The metastatic tumour from the lung showed the same features as the original one. Some of the dissemination in the lung took place through the bronchial tree which was evident (figure 4, plate XVII).

**Discussion and comments.**—Ewing (1931) classified the thymic tumours as follows:—

(1) Lymphosarcoma or thymoma composed of a diffuse growth of round polyhedral and giant cells. The chief source of this tumour is probably the reticulum cell, but lymphocytes are present in large numbers.

(2) Carcinoma arising from the reticulum cells.

To these may be added the very rare and somewhat questionable cases of spindle-cell or myxosarcoma. Crosby (1932) traced the history of the term 'Thymoma' and reviewed the opinion of various authors on the vexed question of the classification of the tumours of the thymus, and further observed that to understand the nature of the neoplastic diseases of the thymus, it is necessary to review briefly the embryology and the histology of the thymus gland. 'At about the second month of prenatal life, the thymus which up to this time was an endodermal organ, begins to be infiltrated with



lymphocytes. These cells migrate into, proliferate among, and separate the epithelial cells of the thymus. It has been shown that the thymic cell is a true small lymphocyte, and it may differentiate into granular lymphocytic cell or into plasma cells; when animals are treated with x-ray, the differentiation is brought about. Some, however, believe that the endodermal cells (endodermal thymic reticulum) differentiate to form the so-called thymic cells'. Kettle (1925) is rather sceptical about the thymic origin of these tumours. He prefers to include these tumours as mediastinal lymphosarcoma originating from the lymphoid tissue, as some of these tumours originate from the posterior mediastinum.

A comprehensive discussion in this subject entails a review of the embryology, histogenesis and pathology of the thymus gland which have been fully dealt with by Foot (1926), Jacobson (1923) and Symmers and Vance (1921).

In the two cases reported above, the main characteristics are the same in both, i.e. the tumours were composed of small round cells with scanty intracellular substance. In none of these could we find any Hassall's corpuscles. It appears that the presence of Hassall's corpuscles is not an essential feature of these tumours (Herriman and Rahte, 1929). With regard to the metastasis Crosby (1932) collected seventy-eight cases of such lymphosarcomatous tumours, and showed that, although the neighbouring organs to the thymus are the usual sites of infiltration, general dissemination was also by no means uncommon. In our case 1, although the tumour was very large, no secondary foci could be found on post mortem. In case 2, the right lung was infiltrated. Besides the usual route of spread, some part of the spread must have taken place through the bronchioles (figure 4, plate XVII). This type of spread appears to be not yet reported.

#### Summary and conclusion

(1) Two cases of thymoma have been reported with metastasis through the bronchioles in one case.

(2) A short discussion as to the histogenesis of this type of rare neoplasm is given.

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## MALIGNANT TUMOURS OF THE KIDNEY

### REPORT OF A CASE OF TUBULAR ADENOCARCINOMA OF THE KIDNEY

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THE pathology of the tumours of the kidney passed through several changes until a clear idea about the origin of the tumours was obtained. The epithelial origin of the tumours was first established by Robin in 1855. Later, yellow coloured tumours of small or large size, well circumscribed, vascular, liable to hæmorrhages, degeneration and cyst formation were noticed in the region of the kidney, which led pathologists to speculate concerning their origin. At first they were thought to be lipomatous in structure until Grawitz in 1883 thought that the structure was identical with the cortical structure of the adrenal tissue.

Various types of tumours, both benign and malignant, have been described. In the majority of cases, malignant tumours are silent for a long time until they assume large proportions and attract the attention of the patient by the discomfort produced and the pressure caused upon the neighbouring organs. Sometimes, however, an early invasion of the tumour into the calices or the pelvis of the kidney causes hæmaturia, frequency of micturition, and sometimes renal colic. When this sign occurs, routine investigation by pyclography may help in the recognition of a tumour. It is unfortunate that this sign of hæmaturia occurs rarely to facilitate early diagnosis.

A pathological study with the clinical correlation has been undertaken by pathologists from time to time. Ewing has tried to classify the tumours according to the morphological structure and their clinical manifestations, and this appears to be a rational classification.

Epithelial malignant tumours may arise from the body of the kidney tissue or from the pelvis of the kidney. The kidney being a glandular organ, tumours arising from this structure, if benign, will be adenomas; if malignant they will be adeno-sarcomas. The following have been described :—

(a) Papillary adeno-carcinoma in which the following sub-varieties are recognized :—

(i) Papillary adeno-carcinoma with clear and glassy cells. Usually these are small tumours, light yellow in colour with considerable vascularity. They form cysts containing a clear brownish, blood-stained and gelatinous material. These are usually found in the medullary portion or in the cortical portion of the kidney and are rare.

(ii) Papillary adeno-carcinoma with granular cells. The tumours may be single or multiple, and appear like a solid white mass in the cortex or medulla of the kidney. These may be found in a sclerotic or normal kidney and bear comparison to the adeno-carcinomas occurring in any glandular organ; they are rare.

(iii) Malignant tumours arising from simple cyst-adenomas. These usually occur in sclerotic kidneys



and are multiple-encapsulated tumours. Most of these tumours are supposed to arise from the renal epithelium, and may represent the renal structure; they are rare.

(b) Alveolar adeno-carcinomas are also recognized from the morphology and structure of the sections of the tumours. Though in some respects they resemble the adrenal derivative, they reproduce to a large extent the renal structure. In this class, there is the adeno-carcinoma of infants, the embryonal adeno-carcinoma of adults, and the tubular adeno-carcinoma of adults. Of these, the first two are less common and the last is stated to be more common. The structure is uniformly alveolar or tubular in type, resembling the renal parenchyma. These tumours may be small or big and when they become big, they enlarge the kidney but preserve its form (*see* the case described below and figure 3, plate XVIII). The growth is uniformly solid, without any fatty changes, hæmorrhages or necrosis. Small cysts containing gelatinous material may be found. When this type of tumour becomes intensely malignant it perforates the pelvis, infiltrates the veins, and produces metastasis in many organs through the blood stream, and this spread may occur early or late. One case is described in this paper in which the tumour was big and resembled the description given above, but with no metastasis.

(c) Embryonal adeno-myo-sarcoma-carcinoma has to be recognized both as a pathological and clinical entity. In this tumour, there is a complex teratogenous structure showing the various types of embryonal tissue in different proportions, the epithelial structure usually predominating in some and sometimes frankly persisting throughout the tumour tissue resembling an embryonal adeno-carcinoma of infants. In others, we find that the epithelial structure is present but not so abundant; it may contain much muscle tissue, nerve tissue, and connective tissue in various grades of proliferation; it may show in some places mitotic figures and hyper-chromatic nuclei giving a complex picture of the adeno-myo-sarcoma.

The clinical picture is very distinct in that it is very common in infants between the ages of 1 and 3 years. Sometimes rare cases are found at the age of 7. It is unfortunate that by the time the surgeon sees this type of tumour, it has assumed very large proportions. Though some are capable of removal, they are intensely malignant. There were 2 cases of this sort in the series.

(d) Of all types of tumours of the kidney, hyper-nephroma is the most common type. Grawitz contended that it originated from the remnants of the adrenal cortex containing light lipid material in the cells, which gave the yellow appearance so characteristic of this tumour. The tumours may be small or big, and are intensely vascular with hæmorrhages and degenerative process leading to cyst formation. When the tumour invades the pelvis it permeates into the veins, thus disseminating by the blood stream to distant parts of the body, especially to bones.

(e) A rare type of malignant tumour is the pure connective tissue tumour known as the sarcoma of the kidney. Very few cases have been reported in literature and Judd has reported one case with a review of 20 cases from the Mayo Clinic. They are considered to be highly malignant.

Eight cases of tumour of the kidney out of 108 cases of diseases of the kidney seen and treated by the author from 1932 to 1943 afforded an opportunity to study the types of tumours that are commonly found.

Of the 8 cases, 2 were embryonal-tumours of the Wilms type in children aged 2 and 3 years respectively. It is unfortunate that no confirmatory operative diagnosis could be made, as the disease was in an advanced state and the parents refused operation.

Of the remaining 6, 5 cases were hyper-nephromas. The ages at which such kidney tumours were found were 30 in both the females, and 39, 45 and 48 in the males. Of the 5, 3 were operated on through a Perthes' incision. This incision had to be used because the tumours were very large, had large venus sinuses, and were found to be fixed and difficult of mobilization. Of the 3 cases operated on, 2 were on the left side and 1 on the right side. The left-sided tumours had varicoceles on that side (figure 1, plate XVIII) but no varicocele was present in the case which had the tumour on the right side. In all the 3 cases, removal was not possible, as the disease was far too advanced and the patient later died of the disease. The 2 cases in the females were not operated on but were diagnosed as hyper-nephromas by the size of the tumours, and the rapid growth with emaciation and pyelographic findings.

The sixth case in a female described below was diagnosed as a case of hyper-nephroma but histopathological examination proved it to be a case of the tubular adeno-carcinoma of adults.

A Hindu female was admitted on 31st March, 1941, for a tumour in the right hypochondriac and lumbar region. She was married and had four children, all healthy. Four months before admission, the patient suffered from constipation and dyspepsia. The patient was given medicine by a general practitioner for three months and then the doctor noticed a lump on the right side of the abdomen and asked the patient to go to a general hospital.

On admission she was found to be a fairly well nourished woman, 40 years of age. There was no anaemia, and general examination revealed no abnormality.

On examination, a lump 5 inches in diameter situated in the right hypochondrium extending to the right lumbar region was noticed. The surface was smooth and the margins were well defined; the lump was quite palpable below the last rib almost to the iliac crest, and medially extended to the lateral margin of the rectus. No fluctuation was present, the mass moved freely on respiration, and the skin over the lump was not adherent. Percussion was dull over the region of the tumour.

Urine examination showed no sugar, no albumin and no crystals, and the stools were free from ova and intestinal parasites. Blood examination showed a normal blood picture.

Ordinary x-ray examination of the kidney region showed nothing abnormal, but a retrograde pyelogram showed the absence of definition of the small calices, blunting and deformity of the lower major calyx, and absence of the lower minor calices (*see* figure 2, plate XVIII).

This patient was operated on under spinal anaesthesia through a Bergmann's incision. On opening the kidney pouch, a big tumour arising from the lower 2/3 of the kidney was seen, with enormously dilated venus sinuses. The kidney was removed after carefully cutting the venus sinuses and the kidney, pedicle between forceps which were released after ligation. The patient stood the operation well. The wound was sutured in layers, with a drain. The patient made an uneventful recovery and was discharged on the 15th day after the operation.

The kidney showed a large fleshy growth replacing more than 2/3 of the lower part of the kidney. It was pale white, and granular, with large venus blood vessels on the surface of the capsule. Spaces which were like clinks suggesting an adenomatous structure were found. There was no degeneration appreciable to the naked eye in the tumour (*see* figures 3, 4 and 5, plate XVIII).

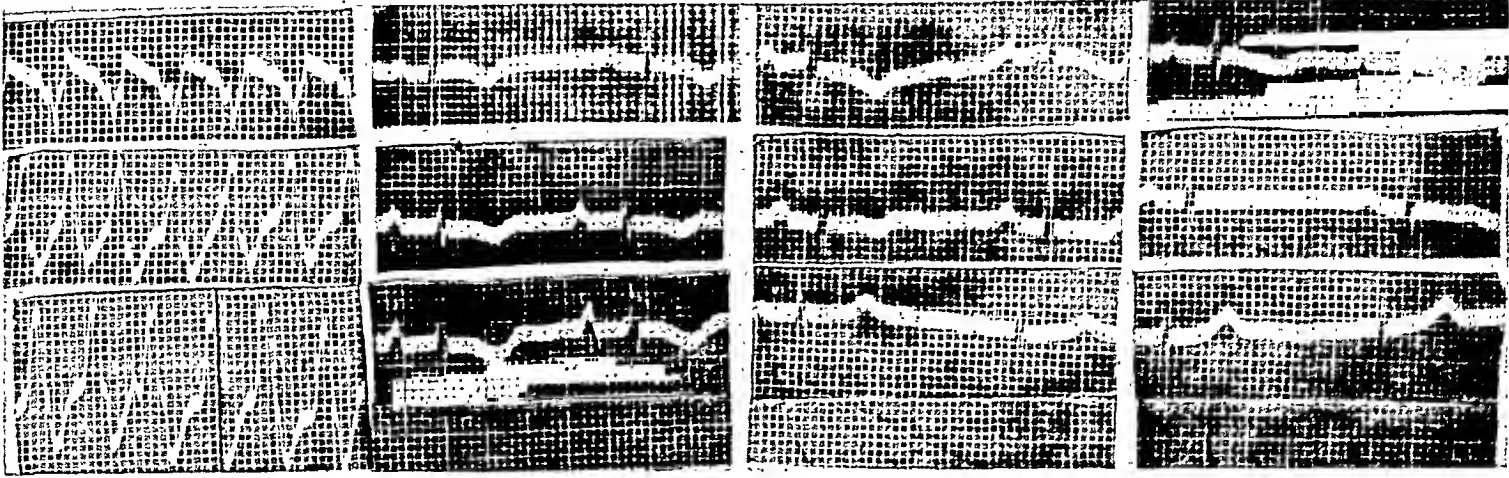


Fig. 1. Fig. 2. Fig. 3. Fig. 4.

Fig. 1.—Electrocardiogram, taken on 27th April, showing paroxysm of ventricular tachycardia. Rate of heart 230 per minute. No dissociation of auricular activity.

Fig. 2.—Electrocardiogram, taken on 8th May, showing resumption of normal sinus rhythm. Rate of heart about 65 per minute. Note inversion of T waves in all the leads.

Fig. 3.—Electrocardiogram, taken on 11th May, showing return of T wave in lead III to normal.

Fig. 4.—Electrocardiogram, taken on 15th May, showing upright T wave in leads II and III and a tendency to return to normal in lead I.

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Fig. 1.—Case 1. Photograph of the tumour. The heart could be seen deeply concealed by the tumour mass

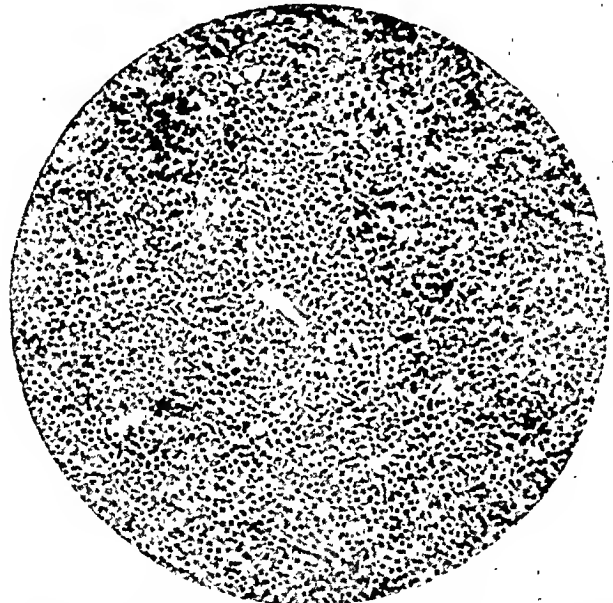


Fig. 2.—Case 1. Photomicrograph of the sections from the tumour. Note uniform character of the cells with scanty intracellular substance.



Fig. 3.—Case 2. Photograph showing tumour. The heart has been pushed

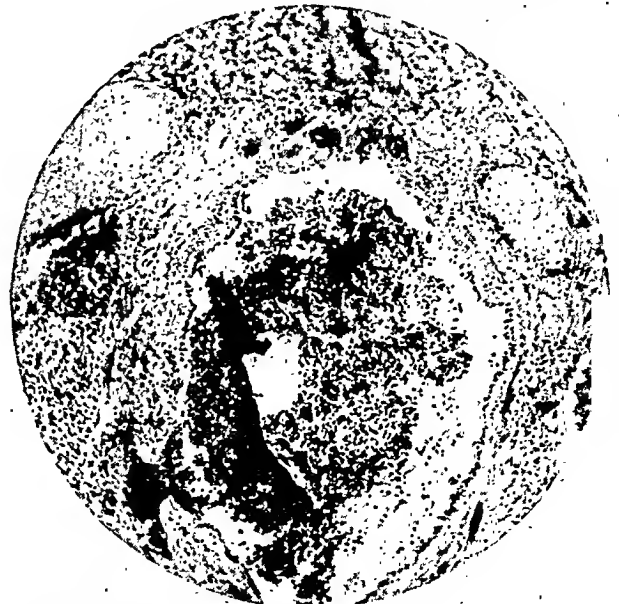


Fig. 4.—Case 2. Photomicrograph of the from the lung tissue showing tumour cells

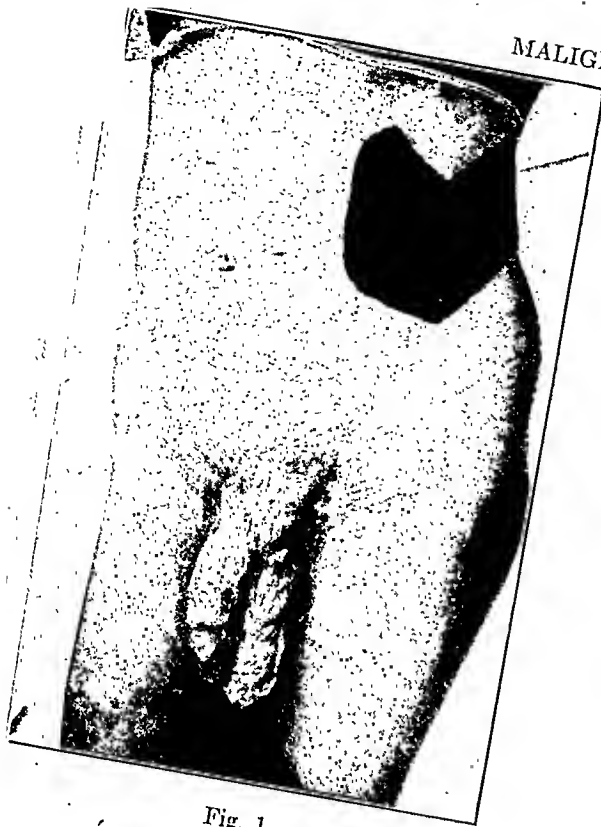


Fig. 1.

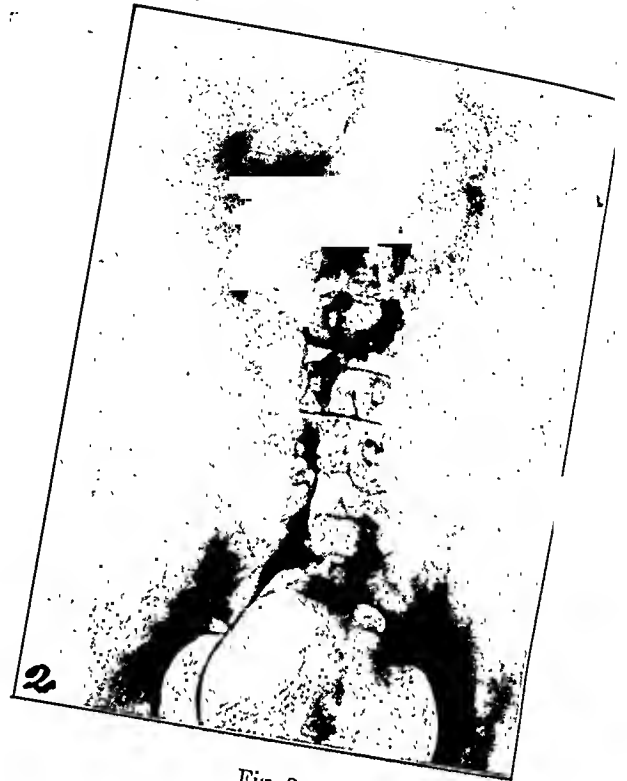


Fig. 2.



Fig. 3.



Fig. 4.

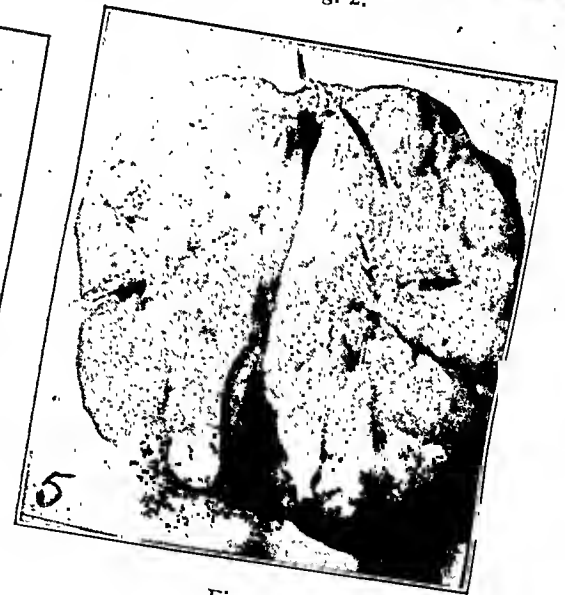


Fig. 5.



Fig. 6.

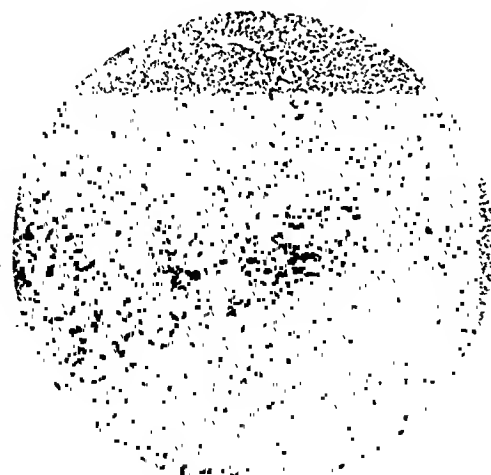


Fig. 7.



Fig. 8.

Histo-pathological examination showed a frank tubular structure with an irregularly scattered alveolar arrangement with marked hyper-chromatic nuclei. Under the high power, the cells appeared columnar with marked hyper-chromatic nuclei (see figures 6, 7 and 8, plate XVIII).

The main complaint of the patient was dyspepsia, and there was no indication of the kidney disease. Was this dyspepsia due to the disturbances in the duodenum caused by mechanical pressure altering the function of the gastro-duodenal tract?

To a letter written in July 1943, the patient has replied that she is keeping good health.

### Summary.

1. A classification of the tumours of the kidney is given.
2. Eight cases of the tumour of the kidney are classified, of which 2 were embryonal tumours, 5 were hyper-nephromas and 1 was a case of tubular adeno-carcinoma of adults.

My special thanks are due to Rao Sahib Dr. K. Narayanan Nair, Pathology Department, Stanley Medical College, Madras, for the micro-photographs.

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### EXPLANATION OF PLATE XVIII

- Fig. 1.—A photograph of a man suffering from hyper-nephroma of the left kidney which was verified at operation. See the remarkable varicocele. The extent of the tumour has been shaded.
- Fig. 2.—A retrograde pyelogram showing the blunting of minor upper calices and deformity of the lower major calyx, with lack of definition of lower minor calices.
- Fig. 3.—A photograph of the specimen removed. Section of the tumour shows a pale white mass with chinks scattered throughout its substance. Note that one part of the kidney appears normal.
- Fig. 4.—Another view of the same specimen showing the dilated venous sinuses. In spite of the large size of the tumour, the shape of the kidney has been preserved though more than two-thirds of the kidney have been replaced by the tumour tissue.
- Fig. 5.—A closer naked-eye view of the sectioned specimen.
- Fig. 6.—A photograph of the patient taken before discharge from the hospital.
- Fig. 7.—A low-power microphotograph ( $\times 70$  magnification) showing the tubular nature of the tumour with hyper-chromatic nuclei.
- Fig. 8.—A high-power microphotograph ( $\times 230$  magnification) showing the columnar cells in frankly tubular structure with hyper-chromatic nuclei.

## PREGNANCY IN A RUDIMENTARY UTERINE HORN

By H. WATERS

MAJON, I.M.S.

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Ectopic pregnancy is a not uncommon condition, but instances of ectopic pregnancy in a rudimentary horn of a uterus are sufficiently rare to merit publication of a case-report.

J. M., aged 27, married 8 months, was admitted on 18th January, 1944, for occasional pain in the right side of the abdomen and backache for one month. She had a swelling in the right iliac fossa and 4 months' amenorrhœa. Her periods were previously regular 3-4/30 type, no dysmenorrhœa. Last menstrual period on 21st September, 1943. Occasional nausea 1½ months later. No swelling of breasts noted.

*On examination.*—She was found to be fat, but otherwise her general condition was good. Breasts—no secretion.

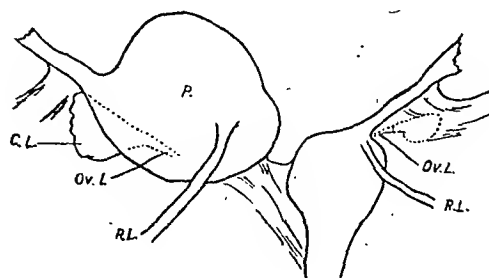
*Abdominal.*—A round swelling rising out of pelvic could be felt in the right iliac fossa, extending 4 inches above the symphysis and 1 inch to the left of the middle line. It was dull on percussion, firm, mobile, and slightly tender.

*Per vaginam.*—Cervix points downwards and forwards, not softened. Uterus upright, small, not softened. Firm round swelling felt in the right fornix and pouch of Douglas separate from the uterus and continuous with the abdominal swelling.

*Blood examination.*—Hb. 85 per cent, R.B.C. 4 millions, W.B.C. 7,000 per c.mm., 58 per cent polymorphonuclears, 41 per cent lymphocytes. The swelling was diagnosed as an ovarian cyst, the amenorrhœa being put down to an endocrine cause in view of the patient's normal sized uterus and her fat condition.

*Operation under spinal anæsthetic on 19th January, 1944.*—The lump was found to be a pregnancy in the interstitial portion of a rudimentary uterine horn. The round ligament, ovarian ligament and tube of the right side were all attached to the swelling, but at points almost equidistant from each other and from the very ill-developed fibrous band connecting the tumour with the other half of the uterus about the level of the internal os. (The more usual condition, of course, is for the tube, round ligament and ovarian ligament

### PREGNANCY IN UTERINE HORN.



P. pregnant horn R.L. round ligament. Ov.L. ovarian ligament. C.L. corpus luteum.

to be attached near each other and at the outer end of the rudimentary horn.) The left-half uterus was small with the left tube and round ligament attached to the top of it. The corpus luteum was in the right ovary (see figure).



The tumour was removed leaving both the tubes and ovaries. A 3½ to 4 months' foetus was found in the gestation-sac the walls of which were thick and muscular. Convalescence was normal.

**Commentary.**—Cases of pregnancy in a rudimentary horn are one of the rarest varieties of ectopic pregnancy, since the sperm has to travel across the uterine cavity to the ovary and tube of the opposite side as in this case. Cases have however been reported, when the corpus luteum was found on the side opposite to that of the pregnant horn. Here it is presumed that the fertilized ovum has made its way across the abdominal cavity to enter the tube of the opposite side.

The diagnosis is not usually made before operation chiefly because the condition is so rare that the possibility of its presence is seldom seriously considered.

The usual course of pregnancy in such a situation is rupture about the fourth month, extremely few cases ever reaching full term. The treatment is therefore removal of the gravid horn as soon as it is diagnosed.

In this case, the marked separation of the insertions of the tube, round ligament and ovarian ligament into the gestation sac show that the ovum must have got embedded at that part of the Mullerian duct where the tube joins the uterine cornua, i.e. the usual site of the rare interstitial variety of tubal pregnancy.

My thanks are due to Lieut.-Colonel Jelal M. Shah, I.M.S., Superintendent, J. J. Group of Hospitals, for permission to report this case.

## DISCOLOURED CHOLESTEROL AND WASSERMANN ANTIGEN

### DECREASED FORTIFYING EFFECT RESTORED BY RECRYSTALLIZATION AND WASHING IN ALCOHOL

By S. D. S. GREVAL

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and

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A SAMPLE of cholesterol (Merck) 5 years old was found to have turned yellow. The general crystalline character, under the microscope, was unchanged, except that the edges of some of the solid rectangles were yellow and in the debris were found yellow cylinders much smaller than the rectangles. The smell was suggestive of bile salts.

The fortifying effect of the sample on the alcoholic heart extract, in the Wassermann reaction, was appreciably reduced.

For the removal of the colour and smell the sample was submitted to four processes: (i) one gramme was subjected to negative pressure in a desiccator—the smell was removed but the colour remained; (ii) one gramme was left in contact with 10 c.cm. of water at room temperature, with frequent shaking—the smell was removed but the colour remained; (iii) one gramme was recrystallized by dissolving in 10 c.cm. of hot alcohol, and the crystals washed on filter-paper in cold alcohol running free of colour, before drying—both smell and colour disappeared; and (iv) one gramme was left in contact with 10 c.cm. of cold alcohol overnight, removed by filtration and washed in cold alcohol running free of colour, before drying—both smell and colour disappeared.

The products of the four processes and two samples from new stocks of cholesterol were left in a desiccator for twenty-four hours for a comparative chemical test and estimation of fortification value with a constant and standardized Wassermann antigen (Greval, Chandra and Das, 1939).

Chemical tests differentiated between the products of (i) and (ii), and the rest. With the former, Salkowski's reaction following Plimmer (Plimmer, 1933) yielded a deep potassium permanganate colour, resembling partly reduced permanganate solution (brown) on the top, and unreduced solution at the bottom; the yellow and green colour did not develop with sulphuric acid. The Liebermann reaction, following the same authority, again yielded a deep permanganate colour with the former. The latter reacted typically.

The fortifying effect on the alcoholic human heart extract of the Wassermann antigen was studied by means of titrated positive controls of syphilitic serum (Greval, Das and Sen Gupta, 1938; Greval, 1943). The controls were 1 in 75 and 1 in 150 dilutions of pooled +++ sera (sera fixing complement with *uncholesterolized* antigen). The stronger dilution was expected to fix 3 MHD of complement completely (+) and 5 MHD incompletely ( $\pm$  or T, trace of lysis). The weaker dilution was expected to fix the same doses to a less degree. The reactions of fixation are given in the attached table. The simplest process of washing in cold alcohol gave the best results. New sample No. 2 gave a slightly higher fixation although this fact is not noted by additional signs in the table.

Other differences of serological importance were also noticed: (i) suspensions in saline from the alcoholic solutions of the discoloured samples were less turbid; (ii) suspensions in saline of the Wassermann antigens made with them were also less turbid; and (iii) the anti-complementary titre of the antigens made with them was slightly higher. These differences disappeared with the removal of the colour.

The importance of saving a chemical not easy to obtain is obvious.

A table giving reactions on seven samples of cholesterol

The Wassermann antigen made with:—	Fixation of complement with titrated positive controls:—			
	Control I, with 3 MHD		Control II, with 5 MHD	
	I, 1, 1 in 75 dil.	I, 2, 1 in 150 dil.	II, 1, 1 in 75 dil.	II, 2, 1 in 150 dil.
1. New stock, Merck	+	T	+	±
2. New stock, B.D.H.	+	T	+	±
3. Recrystallized (process iii).	+	±	+	—
4. Washed in alcohol (process iv).	+	T	+	±
5. Deodorized under pump.	T	±	T	—
6. Washed in water	T	±	T	±
7. Untreated yellow and odorous.	T	±	T	—

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## BACTERICIDAL AND FUNGICIDAL ACTION OF ORGANIC MERCURIALS

### WITH SPECIAL REFERENCE TO THE DERMATOMYCOSES

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With the assistance of

J. H. CROXON  
CORPORAL, R.A.M.C.

It has been stated recently (Hunter, 1943) that the ideal antiseptic should possess high germicidal and inhibitory properties over the widest possible range of the commoner pathogenic organisms, a low tissue toxicity, efficiency in the presence of organic matter, power to penetrate, stability, and moderate cost.

In this country the commoner pathogenic organisms include a great number of mycotic agents, these latter being especially common in moist, humid regions and during the monsoon period. It is therefore considered that the ideal antiseptic should possess a well-marked fungicidal as well as a bactericidal effect. This report intends to show that certain organic mercurial drugs possess the above-mentioned properties in the highest degree, and it is felt that, in the latest spate of literature concerning modern antiseptics, this remarkable series of compounds has been greatly neglected.

Before describing the uses and method of application of the above-mentioned drugs, it would be well to explain the rationale governing the use of antiseptics and bactericidal substances whose active agent is a phenol radicle or Hg cation.

As long ago as 1881, Koch drew attention to the toxic action of mercury on bacteria, and Paul and Prall (1907) showed that this effect depends on the free concentration of Hg ions in solution.

That this Hg cation was the most effective of the heavy metal cations was proved by Woodruff and Bunzel (1909) and later by Winslow and Hotchkiss (1922). This toxic action on bacteria was well manifested *in vitro*, but it has been shown that *in vivo* its bactericidal action is greatly diminished, especially in the presence of organic matter. Chick and Martin (1908) consider that this was due to the fact that these cations combine with protein to form an insoluble albuminate; hence the concentration of free ions is greatly diminished. Clark (1940) reported that when a 3 per cent suspension of dried human faeces is added to a solution of an Hg salt effective *in vitro*, its activity is reduced by 80 to 85 per cent. The activity of certain organic mercurial salts under these conditions is reduced by only 15 to 20 per cent, and that of phenol is reduced by only 10 per cent. It follows, therefore, that in the presence of organic matter, these organic mercurial salts possess a far greater bactericidal effect than those of the inorganic series, while at the same time the phenol co-efficient in the former is far greater than that of the latter. The advantage of using these organic mercurials in tissue lesions due to infection is thus clearly indicated, for it appears that the formation of an insoluble albuminate does not obtain to any marked degree in the use of drugs of this group.

It is proposed to show that the type of organic mercurial employed exerts an influence on the results, on account of varying chemical constitution. The simple aliphatic compounds of Hg have proved extremely toxic in their effect on the human organism. These compounds are represented by the series Hg (R) 2 where R represents one of the lower hydrocarbon radicles. Mercury dimethyl Hg(CH<sub>3</sub>)<sub>2</sub> and mercury diethyl Hg(C<sub>2</sub>H<sub>5</sub>)<sub>2</sub>, the most elementary compounds in the series, have a special affinity for the central nervous system, causing rapid degenerative lesions in cerebral and cerebellar areas. The latter compound is, indeed, one of the most interesting in human toxicology, for there is a latent symptomless period of about 16 days between its application or ingestion and the development of signs and symptoms in the central nervous system.

The higher compounds of the series of organic mercurials (aromatic aryl or tolyl compounds), mainly phenyl mercuric acetate, phenyl mercuric chloride and phenyl mercuric nitrate, have been investigated chiefly in the U.S., but Biskind (1935) gave a detailed account of their action



and reviewed the literature concerning them in an article in the *Lancet* some years ago. (For convenience the above-mentioned compounds will be referred to as P.M.A., P.M.C., and P.M.N. henceforth in this report.)

The bactericidal and bacteriostatic action of P.M.C. was fully investigated by U.S. workers in 1933 and 1934 (Weed and Ecker, 1938). It was found that the concentration necessary to inhibit the growth of *S. hæmolyticus* and *S. aureus* in culture was 1/150,000,000 and 1/125,000,000 respectively.

In England, so far, the above-mentioned compounds have been used chiefly in plant chemistry, and the fungicidal action of P.M.C. was investigated in England by Fitzgibbon using various types of plant fungi. It was shown that this substance is one of the most powerful fungicides known, and acts rapidly and effectively in extremely high dilutions.

Byrne and Fitzgibbon (1932) using 2 per cent P.M.C. on both H.E.B. and diglycol stearate showed that it also exerts a rapid and specific effect on fungi and bacteria pathogenic to man.

In choosing this particular member of the organic mercurial series, the rationale was as follows :—

(1) It was known (Biskind, 1935) that the compound  $C_6H_5HgCl$  had a very high bactericidal potency, with a relatively low local and systemic toxicity for animals and for man.

(2) This effect is due to the action of the compound  $C_6H_5Hg$  ion, and it is thought on theoretical grounds that the bactericidal power of Hg is greatly increased by using it in the form of a phenol derivative.

Experiments by Reichel (1909) on the dispersion phases of phenol between oil and water suggested that the action of phenol is not so much chemical as physical, the phenol being capable of passing into solution in such substances as coagulated albumin, certain lipoids and the cytoplasm of bacteria. He suggested, therefore, that its action results from its penetration into the bacterial cell in the form of a colloidal solution. Moreover, in the presence of serum, no diminution of the germicidal action of phenol occurs (Browning *et al.*, 1917).

(3) Though the solubility of P.M.C. is extremely low, this does not detract from its effectiveness. The active portion is the  $C_6H_5Hg$  ion, and it is considered that this radicle enters into some form of colloidal solution in the cytoplasm of the infecting fungi or bacteria, and hence a continual removal of  $C_6H_5Hg$  ions takes place from the vehicle or filler in or on which the drug is presented to the infecting organism. There appears to be something in the nature of a continual bombardment of the organisms with organically combined Hg. It is considered on theoretical grounds that its effect is to cause a rapid disturbance of metabolic function leading to the death of the infecting agents.

P.M.A. has also been used in the investigation, but as this compound has a marked affinity

for Cl, the change from P.M.A. to P.M.C. takes place immediately on contact with NaCl, and as this latter salt is an invariable constituent of tissue fluid, it was felt that the direct application of the ultimate chemical product should be made. This report, therefore, deals mainly with the action of phenyl mercuric chloride.

As in all bactericides, the reaction velocity of P.M.C. depends on its concentration in the area in which it is to exert its action, but owing to its tendency to produce a vesicant effect on tissue or skin, the concentration used must be carefully limited. If a 1 per cent concentration is applied for some hours to skin lesions caused by bacteria or mycotic agents, an extremely rapid bactericidal and fungicidal effect obtains, but the surrounding healthy skin areas become erythematous or vesicated and do not recover for a further 48 to 72 hours. In practice, it has been found that 0.25 per cent P.M.C. or 0.25 per cent P.M.A. represent the maximum that can be used without producing these effects. Five per cent P.M.C., adsorbed on a calamine filler, can be used on moist skin lesions without side effects, as the physico-chemical mechanisms obtaining when the drug is presented in this way are entirely different from those which occur when emulsifying or aqueous vehicles are used.

This latter method (adsorption of a practically insoluble compound on a filler) is thought to mark a new advance in the presentation of a substance (which is almost insoluble in ordinary media) to the infecting agents on which it is to act.

An alternative method is the preparation of a colloidal solution of the drug, but the grave disadvantage in this method is that, in using colloidal solutions of a drug, the bactericidal activity of which is an ionic property, the protective colloid removes the charge from the active cation and hence nullifies its therapeutic effect.

### *Pharmaceutical Details of the Preparation of P.M.C. and P.M.A. Applications*

(By H. Fine, M.P.S., Sergeant, R.A.M.C.)

Experimental work on the preparations of P.M.C. and P.M.A. applications presented several difficulties, owing to the conditions under which the work was carried out. In an area well forward, facilities for acquiring pharmaceutical elegance were often lacking. Apparatus available was elementary and the only method of registering temperatures was by means of crude, though accurate, improvised thermometers.

It was necessary to consider the physical properties of P.M.C. and P.M.A. very carefully in order that their incorporation into suitable bases would satisfy the following requirements :—

(a) To possess the necessary pharmacological and bactericidal action.

(b) The preparations to be easily made in field dispensaries using the least amount of dispensing apparatus.

(c) The final products to be stable, easily applicable and useable in all the various areas in which the infecting agent was present.

Arising out of the third point, it was decided that, for moist infected areas, a drying lotion would be necessary, and for dry infected areas, an emollient (using an emulsifying base) would suit the case.

Accordingly P.M.C. and P.M.A. were incorporated in three types of base :—

- (1) In a Eucerin and distilled water base;
- (2) In an adhesive lotion of the calamine lotion type.
- (3) In simple solution in distilled water.

#### A. Eucerin and distilled water base.

P.M.A. is soluble in hot distilled water up to a concentration of 1.5 per cent.

P.M.C. is practically insoluble in water.

It was found that two methods were necessary in order to incorporate P.M.A. and P.M.C. in this emulsifying base.

##### (a) Phenyl mercuric acetate (P.M.A.)—

P.M.A.	..	..	0.125 per cent.
Eucerin	..	..	3 parts.
Distilled water	..	..	5 "

The P.M.A. is dissolved in distilled water heated to 85°C. This solution, while still warm, is slowly added to the Eucerin previously melted and kept at a temperature not exceeding 55°C. The mixture is continuously stirred until cool, when a white homogeneous cream is produced, which is easily absorbed into the skin with the minimum of friction.

##### (b) Phenyl mercuric chloride (P.M.C.)—

P.M.C.	..	..	0.20 per cent.
Eucerin	..	..	3 parts.
Distilled water	..	..	5 "

As P.M.C. is practically insoluble in water, the most efficient method is to incorporate the P.M.C. with the melted Eucerin at 55°C., using careful trituration and keeping the contents of the mortar heated to 55°C. by means of a water-bath. It is essential that the P.M.C. be as evenly dispersed as possible in the melted Eucerin before adding the distilled water (heated to 85°C.) in small quantities, with constant stirring. The whole is now allowed to cool rapidly, stirring until a white homogeneous cream is obtained. This product, too, is quite easily emulsified into the skin.

Even more perfect diffusion of the active constituent could be obtained if the final product could be put through a homogenizer of the 'Empire' hand type. Unfortunately, owing to the limited apparatus available, this could not be done in this dispensary.

#### B. Adhesive lotion base

For moist surface infections, it was decided to use local treatment to the affected areas by means of a lotion which was capable of :—

- (1) Being applied in sufficient concentration to exert the maximum bactericidal action.
- (2) Enabling the area to be gradually dried.

(3) Preventing any aggravation of irritation and, if possible, have the maximum cooling effect.

(4) Remaining in contact with the area for a prolonged period, although the area may be constantly moist, due to perspiration.

(5) Being easily applied.

All these conditions were satisfied in the product of the following formula :—

P.M.C. 0.5 per cent impregnated on			
calamine B.P.	..	..	gr. xv
Zinc oxide	..	..	gr. xxx
Glycerine	..	..	m xxx
Aquam ad.	..	..	1 oz.

A supply of calamine impregnated with 0.5 per cent P.M.C. was supplied by the courtesy of Lunevale Products Laboratories.

Probably owing to the method of preparation, the impregnated calamine was found to be very much more dense than calamine B.P., and thus required a large amount of zinc oxide and glycerine to maintain an even suspension when shaken, and sufficient adhesiveness when applied to the infected area. The method of preparation is identical with that of calamine lotion, although it must be stressed that the two insoluble powders must be very carefully mixed and sifted before adding the glycerine and required amount of water.

#### C. Solution with distilled water

For large infected areas of deep seated origin, and for open infections of the 'jungle sore' type, it was found that an application of a solution of P.M.A. had the desired therapeutic effect. Varied concentrations were tried and the following solution found to be the most satisfactory :—

Phenyl mercuric acetate	..	0.05 per cent.
Sterile distilled water	..	5i

Solution is effected by heating up 2 grammes of P.M.A. in 250 c.c. of distilled water and pouring the almost boiling solution into 750 c.cm. cold distilled water. Stir well and allow to settle. Filter from sediment of which there will be traces. This stock solution can be regarded as 0.2 per cent W/W or W/V for all practical purposes. The desired strength of solution may then be obtained by further dilution with the required amount of cold distilled water.

Owing to the extraordinarily high phenol coefficient of P.M.A., conditions for making this solution do not necessitate the use of rigid aseptic precautions, as even in this dilution it is found that the solution is itself self-sterilizing.

A survey of the above methods of making P.M.A. and P.M.C. preparations shows that it is within the scope of any dispensary in the field to dispense these preparations. They are easily and quickly made, and the final products are quite 'elegant'.

#### Methods of application of the above preparations of P.M.C. and P.M.A.

At the beginning of the investigation, the cases were treated as follows :—

Cases from the Convalescent Wing of the C.C.S. where this work was carried out were

treated as out-patients, attending at the M. I. Room twice daily, where thorough inunction of P.M.C. ointment was carried out. Though results were very satisfactory, it was found that the method was wasteful in the use of the limited amounts of ointments at our disposal, and so all the convalescent cases were admitted for 1 to 2 days to the Skin Section of the C.C.S., where the ointment was applied on lint and bandaged on to the affected areas.

As the reaction velocity of P.M.C. depends both on the concentration applied and the duration of application, it was found that the latter method mentioned above effected a great saving in the amount of ointment used, and produced a much more rapid curative effect. It was later found that if the method of application outlined below is carefully adhered to, hospitalization of infected patients is quite unnecessary.

The types of mycotic infection observed, affecting the trunk and limbs, varied enormously, presumably due to the nature of the infecting fungus, and the skin reaction of the patient. It is considered that variants occur in the strain of fungi akin to those occurring in bacterial infections in man. Dry, superficial, circinate infections of large extent and rapid spread alternated with those producing agminate folliculitis; and maculo-papular lesions of both guttate and punctate varieties were found. Epidermophyton infections, i.e. *E. inguinalis* and the so-called 'foot-rot', are among the commonest lesions met with. As stated above, the type of application varied with the nature of the lesion and in general the following principles of treatment were adopted:—

(1) '*Agminate folliculitis*'.—One application of 0.20 per cent P.M.C. was used on lint, after thorough cleansing of the affected part. The ointment was left in contact with the lesion for 3 to 4 hours after inunction.

(2) '*Dry spreading, circinate lesions*'. A four hours' application of 0.20 per cent P.M.C. on lint was carried out, and for the raised maculo-papular type of lesion, this treatment also proved eminently successful.

Occasionally, some small lesions of the guttate type proved resistant to treatment. 0.25 per cent P.M.A. in chloroform applied to these caused a rapid resolution, though in a few cases a temporary vesication was produced. In view of the extreme rapidity of the control of the infection, this latter effect (which was quite mild) was not considered to have any detrimental action, and all side effects cleared up in 24 to 48 hours.

For moist open lesions, preliminary treatment with (0.20 per cent) P.M.C. on lint for 3 hours was used, followed by the P.M.C. lotion (0.5 per cent adsorbed on calamine). Clearance of the lesions occurred in 2 or 3 days.

#### *Epidermophytosis of the feet*

The interdigital spaces were thoroughly cleaned and all dead skin was removed. 0.5 per cent

P.M.C. on calamine was used in powder form where moist lesions occurred and when the area was dry (usually 24 hours after the powder application) 0.20 per cent P.M.C. ointment or 0.125 per cent P.M.A. ointment was used. It is essential to keep a careful check on the state of the lesions, and to vary the powder, lotion or ointment in order to keep the skin in its normal condition.

#### *Epidermophyton inguinale* (dhobi itch)

This type of infection was treated by one application of 0.20 per cent P.M.C. After thorough inunction into the affected areas, with special attention to the infected spreading edge, strips of lint coated with the ointment were applied to the lesion and fixed in position by means of pads of cotton-wool and a double T-bandage. Four hours' application was usually sufficient to cause complete disappearance of the lesion. Regarding epidermophyton infections of the toes, recurrences are mainly due to the following causes:—

- (i) fresh infection from an outside source and
- (ii) re-infection from the socks or the footwear of the patient.

The spores of the causative fungus remain in or on the patient's socks or footwear, and are not destroyed in washing (by the usual dhobi method). It is essential to steep the socks overnight in 1/1,000 perchloride of mercury or, better still, 1/2,000 P.M.A. solution to ensure thorough destruction of spores. The socks can then be rinsed and washed in the usual manner. Some spores remain in the boot or shoe and, as treatment in a disinfector renders these articles unserviceable for further use, it is suggested that thorough treatment with 1/1,000 P.M.A. solution will rapidly render them free from spore contamination.

#### *'Jungle sores'*

Preliminary local cleansing with removal of all dead organic matter from the affected part was carried out. 1/2,000 P.M.A. compresses were applied for 6 hours, to thoroughly disinfect the lesions; elastoplast was then applied. Extremely rapid healing occurred, as both bacterial and mycotic infecting agents had been destroyed and the sores rendered practically aseptic.

For open infected wounds of all varieties, application of dressings soaked in 1/2,500 P.M.A. gave rapid and excellent results, the infected area being completely disinfected in 24 hours. All dead organic matter must be removed as far as possible before applying this solution.

The number of open infected wounds treated was small, but results were rapid and spectacular. A fuller investigation of the effects of P.M.A. on these conditions is now proceeding, and a report will be published later, when a number of cases sufficient to show results of significant statistical value has been treated.

In some of the dermatomycoses recorded above, 0.125 per cent P.M.A. ointment was used. The results differed in no way from those effected

by P.M.C. The method of application and period of contact employed was the same for both compounds.

Following application of the above ointments, slight and temporary vesication may be seen in some cases, especially round the spreading edges of the lesion, but this disappears after 24 to 48 hours, leaving a clean healthy skin beneath. Secondary infection does not occur, as the minute vesicated areas remain aseptic in view of the powerful antiseptic action of the compound used.

#### Number of cases treated

##### Classification—

(i) Ringworm of trunk and limbs ..	115
(ii) Tinea cruris ('dhobi itch') ..	62
(iii) Epidermophytosis of feet ..	20
(iv) 'Jungle sores' ..	32
(v) Infected wounds of various types	21

In groups (i) and (ii) a single application of 0.20 per cent P.M.C. or 0.125 per cent P.M.A. for 3 to 4 hours caused complete healing of the mycotic lesions. In group (iii) 2 to 5 days was sufficient to bring about clearance of the disease. In group (iv) after preliminary application of 1/2,000 P.M.A. disinfection of the lesions occurred and the application of elastoplast gave rapid and satisfactory results. In group (v) the small number of cases so far treated have shown extremely promising results, and further investigation in an extended series of cases is now being carried out.

As regards group (iii) it was found that when the infection was seen at an early stage, 24 to 48 hours' treatment with 0.5 per cent P.M.C. powder was sufficient to effect cure. Where a superimposed cheiropompholyx is present, somewhat slower curative effects obtain.

It must be emphasized that the rapid cure of epidermophytosis of the interdigital spaces is only possible when the lesion is seen at a reasonably early stage. Many cases have been seen where this infection has been present for years; in these cases hyperkeratosis and fissures are present, and it is quite impossible to effect permanent cure by the above methods of treatment, the reason being that while a temporary cure is effected by the destruction of the vegetative form of the fungus, the resistant spores remain below the hyperkeratotic areas. No matter how effective the fungicidal agent used and how efficient the emulsifying base in which it is presented, the conditions obtaining in the chronically infected areas do not permit of the effective destruction of the spores of the responsible mycotic agent, and relapses are bound to occur.

X-ray therapy represents the only efficient method that can effect permanent cure in these cases.

As regards the types of application mentioned above, it is essential that the method of application and duration thereof be strictly adhered to in order to effect that rapid cure which has been described.

#### Summary and conclusions

(a) Phenyl mercuric chloride and phenyl mercuric acetate in plant mycology are recognized as possessing specific and rapid fungicidal effects in high dilution.

(b) Similar effects obtain in the case of the fungus infections occurring in man.

(c) The bactericidal potency of these drugs is extraordinarily high, and work is being carried out on their action as surface antiseptics. Preliminary results are extremely satisfactory.

I wish to thank Lieut.-Colonel P. D. Johnson, R.A.M.C., O.C., 9 British C.C.S. (at which unit most of this work was carried out), for permission to publish this report. My thanks are also due to Mr. M. Fitzgibbon, F.I.C., Lunevale Products Laboratories, Lancaster, U.K., for generous supplies of P.M.C. and P.M.A. and for the special calamine preparations referred to, and for his helpful suggestions regarding certain technical details. I am also indebted to Sergeant H. Fine, R.A.M.C., for his work in the preparation of P.M.C. and P.M.A. applications.

This investigation would not have been possible without the painstaking and detailed co-operation of the orderlies in the dermatological section, to whom I must pay a special tribute for their excellent work.

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#### A METHOD FOR DETERMINING THE TEMPERATURE OF AUTOCLAVES DURING STERILIZATION

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WITH the starting of the Blood Bank in Calcutta, the responsibility for sterilizing daily a large variety of material fell on us. As we did not have any large industrial type of autoclave suitable for the purpose, we had to work with a number of small autoclaves that were available. These were of different sizes, makes, and patterns, and it was felt that, before putting

them into use in an important work of this kind, we should test their efficiency, especially as in certain instances there was a suspicion that the sterilization was not always quite efficient. We therefore wished to obtain information on the following three points about each autoclave: (1) the accuracy of the pressure gauge, (2) the time taken for complete air displacement, and (3) the time taken by large sized, poor heat-conducting articles to attain the temperature of the autoclave.

A study of these questions revealed that, if we had an accurate method for determining the temperature of autoclaves during sterilization, we could easily obtain the information needed on all three points. Although various methods have been described for the purpose by different workers (Hayes, 1937; Rishworth, 1938; Willan, 1940; Spooner and Turnbull, 1942), most of these were considered unsuitable for our requirements. Underwood (1934) had used thermocouples but he gave no details about his technique. As the 'thermocouple' method was considered particularly suitable for our investigation, we decided to adopt a technique used by Dyer, Sankaran and Subrahmanyam (1943) for testing the temperature of their serum drying plant, with certain modifications. This article describes the method employed, the answers to the three questions elicited by its use, and their bearing on the sterilization work of blood banks.

#### *Thermocouple method of determining temperature of autoclaves during sterilization*

Copper constantan thermocouples were employed. Fine wires S.W.G. no. 38 for copper, and uncovered 38 gauge for constantan (also called Eureka) were used in sufficient length to reach from the bottom of the autoclave to about a yard outside it. The autoclave ends were joined by twisting, were placed at the desired position inside the autoclave, and generally tied to the article whose temperature was to be determined. From there, the wires were taken out underneath the lid of the autoclave, taking care to keep them from touching each other at any place other than the junction already made. Insulation from the metallic lid of the autoclave was secured by covering the wires at the place of contact by thin sheets of dry cellophane paper. The cellophane paper was changed whenever it was found wet after use. Dyer, Sankaran and Subrahmanyam (*loc. cit.*) introduced the thermocouple wires through a special hole in their desiccating chamber, but as we did not like to bore holes in our autoclaves, this simple device of introducing the wires under the lid of the autoclaves after insulation with cellophane paper was adopted and proved quite satisfactory. No leakage of steam occurred due to this procedure. The outside ends of the thermocouple wires were joined to long silk-covered copperflex wires which were in turn joined to the terminals of a Tinsley's potentiometer kept in an adjoining

room free from the heat and moisture of the autoclave room. The junction of the constantan wire with the flex wire was kept in melting ice contained in a thermos flask. The potentiometer was connected to a 2-volt accumulator through a rheostat, and also to a Hartman and Braun moving coil galvanometer of sensitiveness 10-9 amperes. The potentiometer was thus capable of reading up to 10 micro-volts. As there was no standard cell to standardize the potentiometer, a separate copper constantan thermocouple acting between boiling distilled water (100°C.) and melting ice (0°C.) was used as the standard E.M.F. This is known to give 4.275 milli-volts, and so before every reading the potentiometer was standardized for this value. The accuracy of this method was tested, using a water bath and a standard mercury thermometer, and the difference in values was found to be within  $\pm 0.5^{\circ}\text{C}$ . From the value of the E.M.F. generated by the thermocouple of the autoclave, the corresponding temperature was deduced by reference to a graph giving the E.M.F. temperature relationship for copper constantan thermocouples. The temperature that pure steam should give at the pressure indicated was also obtained from a graph, and the two values of temperature were compared and the corrections applied to the pressure gauge. By using more than one thermocouple in the same autoclave, and by putting the desired couple in connection with the potentiometer, readings at different positions in the same autoclave could be taken without changing the rest of the experimental set-up.

Using this method we tested the accuracy of the pressure gauges, the time taken for displacement of air and the time taken by the large sized, poor heat-conducting articles to attain the temperature of the autoclave. The results are given below:—

#### *I. Accuracy of pressure gauges*

In all, 6 autoclaves belonging to the Institute and one belonging to another institution were tested. On each of them 3 to 12 examinations were conducted. Out of the 7 autoclaves tested, 2 required gauge correction. The type of data obtained for satisfactory and unsatisfactory gauges are given in tables I and II.

It is common knowledge that for effective sterilization the temperature inside the autoclave is of primary importance. In view of the difficulties associated with the recording of temperature inside autoclaves, these are fitted with pressure gauges so that the temperature can be determined indirectly from the pressure recorded, using the temperature pressure relation of pure steam. The errors that are likely to arise by the use of pressure gauges however are two: (1) inadequate displacement of air from the autoclave may result in a pressure for the steam less than that indicated on the gauge by an amount equal to the undisplaced air. In such cases the actual temperature inside the autoclave will be



TABLE I  
*Satisfactory gauge*

Time	Steam nozzle	Pressure gauge — reading	Potential of standard thermo-couple	Potential of autoclave couple	Temperature as per pressure gauge	Temperature as per thermo-couple	Variation
1-50	Open steam just issues.	0	4.275 m.v.	4.260 m.v.	100°C.	100°C.	<i>nil.</i>
1-55	Closed (air displacement complete confirmed).	0	4.275 m.v.	4.275 m.v.	100°C.	100°C.	<i>nil.</i>
2-10	Do.	$\frac{1}{2}$ atm.	4.275 m.v.	4.90 m.v.	113°C.	114°C.	+ 1°C.
2-30	Do.	1 atm.	4.275 m.v.	5.35 m.v.	121°C.	122°C.	+ 1°C.
2-45	Do.	$1\frac{1}{2}$ atm.	4.275 m.v.	5.69 m.v.	130°C.	130°C.	<i>nil.</i>

TABLE II  
*Unsatisfactory gauge*

Time	Steam nozzle	Pressure gauge reading	Potential of standard thermo-couple	Potential of autoclave couple	Temperature as per pressure gauge	Temperature as per thermo-couple	Variation
1-39	Open steaming	0	4.275 m.v.	4.27 m.v.	100°C.	100°C.	<i>nil.</i>
1-59	Closed (air displacement complete confirmed).	5 lbs.	4.275 m.v.	4.52 m.v.	109°C.	106°C.	- 3°C.
2-12	Do.	10 "	4.275 m.v.	4.85 m.v.	115°C.	112°C.	- 3°C.
2-25	Do.	15 "	4.275 m.v.	5.07 m.v.	121°C.	117°C.	- 4°C.
2-32	Do.	20 "	4.275 m.v.	5.32 m.v.	126°C.	123°C.	- 3°C.

less than that indicated by the pressure gauge, (2) inaccurate calibration of the gauge either during its manufacture or due to constant use over a long period may give wrong readings and lead to inefficient sterilization. In the experiments recorded above, we made sure that all air had been displaced before testing the accuracy of the pressure gauges. For defective gauges a correction slip was prepared based on the data collected, and its adoption ensured efficient sterilization. It seems therefore advisable to test the pressure gauges of autoclaves before using them in very important work such as that of blood banks.

## II. Time taken by different autoclaves for displacement of air

With the same thermocouple method, a number of experiments were done in which various time periods were allowed for the displacement of air from autoclaves, and for each period the temperature pressure relation was determined. The time required for complete displacement of air was inferred from the results. The time required varied from 1 to 10 minutes. The leaky autoclaves took less time to displace air than the non-leaky ones, as during the period in which

the pressure rose to the required value, the air escaped through the steam outlet as well as through the leaks. Since all these experiments were conducted after loading the autoclaves with different types of material, it may be concluded that a maximum of 10 minutes should be allowed for air displacement. For autoclaves of sizes ranging from 8 inches by 18 inches to 20 inches by 30 inches, and with similarly placed and sized nozzles and gas burners, this period should suffice.

As incomplete displacement of air from autoclaves leads to inefficient sterilization, it is essential to ensure that all the air has been displaced from the autoclave before closing the steam outlet valve. Different autoclaves under different conditions take different periods to displace air, and therefore it is necessary to find out the maximum and minimum time taken by an autoclave to expel all air under different conditions of loading. If this is done, then suitable instructions can be given to those in charge of sterilization work. In most laboratories, sterilization is entrusted to laboratory assistants, and they need to be given definite instructions on such points or else they are apt to make mistakes.



### III. Time taken by large sized, poor heat-conducting articles for attaining the temperature of the autoclave

The thermocouple method was also used for determining the temperature lag produced by the poor heat-conducting material and the extra time of sterilization needed to compensate for this. Ten litre bottles, 10 inches by 18 inches, containing normal saline, and one pound bottles, containing thick filter-paper pulp, were used for this study. The former showed a temperature lag of 21° when the temperature of the autoclave was 120°C. and took 50 minutes more to reach 120°C. The latter (filter-paper pulp) showed a lag in temperature of 12° and took 40 minutes to reach 120°C. These findings emphasize the necessity for longer periods of sterilization than are commonly employed. These results have helped us greatly in modifying the sterilization periods for different materials and in obtaining better results. For important work such as that of blood banks, it is necessary to bear this in mind and to prescribe appropriate sterilization periods.

#### Conclusion

A thermocouple method of testing the temperature of autoclaves during sterilization is described.

It has been successfully employed for testing the efficiency of autoclaves, and for obtaining data on which to base appropriate instructions for correct working when different materials are being sterilized.

It is recommended that autoclaves used by blood banks should be periodically tested by a method such as the one described in this article.

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## REGULATION OF THE CONTROL OF ANOPHELES OF THE FLUVIATILIS-GROUP BY ANTI-ADULT SPRAYING

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THE *fluviatilis*-group consists of the three species: *fluviatilis*, *varuna* and *minimus*. All three are proved malaria carriers of great potency in India. *A. minimus* further extends across the

hills of the Burmese frontier into French Indo-China and Southern China as far as Hong Kong (Toumanoff, 1936). The importance of this species in the war against Japan requires no emphasis.

The adult habits of *minimus* have been studied by Thomson (1941), and of all three species by the present first author (unpublished). Among Muirhead Thomson's conclusions from his experiments are the following:—

(a) During the hot damp monsoon, *A. minimus* takes two days to digest its blood meal and develop its ovaries, ovipositing on the second night after feeding. In cold weather conditions, this period is increased to from four to six days.

(b) At sundown there is a strong attraction to light, and most mosquitoes leave the house at this time. There is no similar reaction at dawn.

(c) Marking and other experiments show that there is a considerable daily turn-over of the population in houses.

(d) About 90 per cent of blood feeding takes place after midnight. After oviposition, *A. minimus* returns for another blood meal on the same night.

(e) In fertilized females, one blood meal is sufficient for egg laying.

The present first author has had in progress for the last two years a series of experiments designed to extend Muirhead Thomson's work and to observe the effect of spraying on the numbers and behaviour of eight species of anopheles, including all three species of the *fluviatilis*-group. These experiments are nearing completion, but the analysis and discussion of the mass of data obtained will take some time. Meanwhile the world supply position in respect of insecticidal sprays has become so acute that it is felt that the practical application of the findings from the work of Muirhead Thomson and of myself should be published in brief, as efficient control of the group can be achieved without the enormous expenditure of insecticide which is causing the present shortage. Put very briefly, the present first author's findings in respect of the *fluviatilis*-group are:—

(i) In a house 'caught to emptiness' daily, 96 per cent of the *fluviatilis* and *varuna*, and 100 per cent of the *minimus* population the next morning is fresh fed.

(ii) If the mosquito population is disturbed by catching to emptiness only once weekly, in *fluviatilis* and *minimus* 82 per cent is fresh fed and 94 per cent in *varuna*.

(iii) With all three species the number found resting in empty houses is no more than 11 to 15 per cent of those found in inhabited houses.

(iv) In a house 'baited' only with a cow, the *fluviatilis* population is no more than 16 per cent of that in a similar house with a human bait, but the percentage is increased to 50 in *minimus* and to almost equal numbers in *varuna*. However, as the anthropophilic index of *varuna* so caught is 67 per cent, compared with 81 per cent in those caught at human bait, it is obvious

that most of the specimens (which are all freshly fed) caught near cattle are only resting there after recent human feeding nearby, i.e. they are in the first 24 hours of the digestion cycle, during which the other members of the group are very much less inclined to move.

(v) Classifying captures by 'wing stages', and counting stages III and IV as 'old', the number of old, i.e. potentially infective, individuals is reduced by daily spraying by 71 per cent in *fluvialis*, and to nil in *varuna*. Throughout the two years of the experiments so few (by this criterion) old specimens of *minimus* have been captured that it cannot be applied. Daily spraying halves the total numbers in *fluvialis* and *varuna* but in *minimus* reduces them by 27 per cent only.

With once-a-week spraying, the 'old wings' are reduced by 66 per cent in *fluvialis* and by 38 per cent in *varuna*. As stated above, this criterion cannot be applied to *minimus*. As regards numbers, once-a-week spraying causes in all three species an increase in numbers resting as compared with an unsprayed house of exactly similar construction and baiting. This phenomenon is not found with *culicifacies* in the same set of experimental houses, and so is not caused by the human bait in the sprayed rooms being more attractive than in the comparison room. It is quite un-understood at present.

From these findings the following conclusions may be drawn :—

(A) There is in all three species of this group an almost complete daily turn-over of the individuals in a house. This means that insects which have fed one night have left the next. This confirms and extends Muirhead Thomson's conclusion (c). Departure is not delayed by lowered temperatures, even though digestion is.

(B) Except in the case of *varuna*, only a small proportion of the departing individuals pass from houses to cow-sheds or to empty houses. Wherever they move to generally, it is to spots where they are inaccessible to spraying. An individual of the *fluvialis*-group is therefore only 'vulnerable' for one daylight period in each digestion-ovarian cycle, irrespective of the length of this.

(C) In areas such as the hills of the Central Provinces where *varuna* forms a considerable percentage of the total numbers in the group, it is worth including cow-sheds in the spraying programme.

Taking into consideration Muirhead Thomson's finding (a) with my finding (B), there is, in the hot damp season, a bite by an individual of this group every 48 hours, the interval extending to 96 hours or longer as the weather cools. After this bite, which takes place between midnight and dawn [Muirhead Thomson's conclusion (d)], the insect remains in the house until dusk of the same day [Muirhead Thomson's conclusion (b)]. It then goes outside until it oviposits, when it returns around midnight or later to feed again. This time-table, incidentally,

shows the futility of spraying before going to bed, as a measure of malaria prevention where this group of anopheles is concerned. At the ordinary camp bedtime there are practically no specimens of the group in houses.

In figure 1, these in and out movements are indicated by horizontal lines in which the breaks indicate the non-vulnerable outside periods. As insects enter every night, eight nights' entrances and movement cycles of mosquitoes A to H are delineated, but the number of entrance cycles is, of course, limited only by the life of the insects. Digestion-ovarian cycles are not shown for periods taking longer than 96 hours to complete, as it is believed that such only occur at temperatures lower than 60°F., during which the sporogony cycle of the malaria parasites is inhibited (Jancso, 1904; Knowles and Basu, 1943).

In malaria transmission, we have to consider equally the parasite as well as its vector, for temperature affects the length of the sporogony cycle as well as, though differently to, the ovarian cycle in the insect. The latest determinations of the sporogony cycle under different temperature conditions are those of Knowles and Basu (*loc. cit.*). These authors worked with *A. stephensi*, and for lack of any evidence to the contrary it must be assumed that difference in vector species does not affect the results. These authors found as under for the period from infective feed to gland invasion by sporozoites (in days).

°F.	<i>P. vivax</i>	<i>P. falciparum</i>
50	nil	nil
60	18	nil
70	15	14
80	11	10
90	9	9
100	nil	nil

Now the rationale of spray control is to destroy the insect before it becomes infective to man (Thornton, 1935). We cannot take into consideration differences in the length of the development cycle in different species of parasite, but must work against the shortest cycle possible for any species at the temperature under consideration. Therefore, in the monsoon, we must destroy the mosquito before the 9th day, in the autumn before the 10th day, and in winter before the 14th day. The actual dates covering these seasons will differ in different areas, and in control work will require regulating by meteorological observations. In the figure, the oblique line drawn through each movement graph indicates the point at which an insect first entering and obtaining an infecting feed itself becomes infective. Before this point is reached the figure shows that it is four times vulnerable on the 48- and 96-hour digestive cycles, and thrice on the 72-hour cycle. So long as spraying is done every day, there is no fear that it will

not be subjected to the chance of more than one 'hit' before the infective stage is reached, but it is hardly possible under present conditions of supply to expend pyrethrum extracts indiscriminately on this basis, even when considerations of cost do not apply. Yet when we come to advise spacings of spray rounds (indicated by + in table I) to catch all the various movement cycles arising from nightly mosquito

I have classified the round so devised as under:—

- 3—3; spraying on 3 consecutive days followed by 4 days no spray.  
 2—1—2; 2 days spray, 2 days no spray, 1 day spray, 2 days no spray, 2 days spray. Repeat *ab initio*, i.e. after 2 days no spray, recommence 2 days spray.

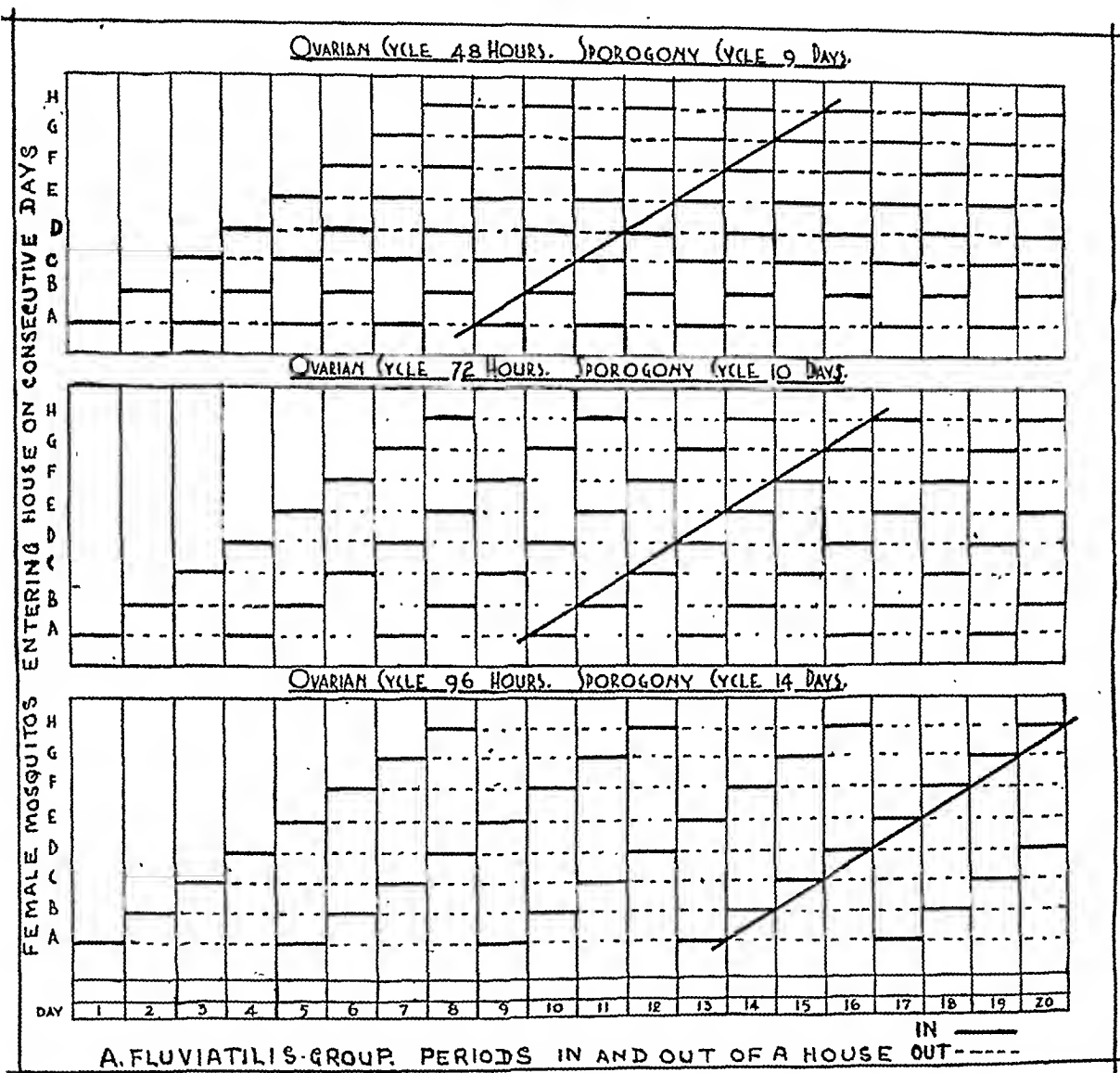


Fig. 1.

entrancees and varying outside resting intervals, we encounter some difficulty. The spacing of spray rounds shown in table I has been arrived at by inserting drawing pins in various permutations in the figure and are designed as far as possible to afford two chances of a hit before the glands are invaded, irrespective of the day of entrance in relation to the day on which spraying is begun. With thorough spraying by trained personnel few insects should escape two attacks.

- 1—1; every other day spray.

- 1—1; 1 day spray followed by 2 days no spray.  
 2

Table I presents two solutions for each digestion-ovarian eye cycle varying with temperature, and the corresponding sporogony cycle, devised for less and for more intensive, and expensive, control, as local conditions may rule. It is not claimed that better spacings could not be found. Anyone interested is recommended to restfully



try and devise such in lieu of doing a crossword puzzle!

The best way of obtaining evidence as to results of malaria control by any entomological method is by dissection. In the first place, therefore, results from 6 days a week spraying are given as a comparison:—

*Gua* (Singhbhum Hills). Thirty sprayed railway quarters compared with 30 adjacent unsprayed mines quarters. Spleen rate of latter (October 1943) 78 per cent. Figures for once-weekly catches over 26 months:

	UNSPRAYED QUARTERS			SPRAYED QUARTERS		
	Number	Oöcyst rate	Sporozoite rate	Number	Oöcyst rate	Sporozoite rate
All 3 species	1,112	4.7	3.5	46	4.3	2.2

The reduction in density is 24 : 1. The infection rate of insects escaping the spray is not affected, and it is obvious that in this group malaria control is achieved by reducing density. If the insect is not destroyed, the survivors are relatively just as dangerous as if no spraying was done.

As a result of the above measures, malaria incidence in the railway staff between July and December were:

1938-1940. No control .. 27 per cent

1941-1943. Spray control .. 11 "

To illustrate the results of spaced spraying: *Posoita* (Singhbhum Hills). Thirty sprayed railway quarters compared with 8 rooms in a

at this small jungle station has varied from 86 to 90 per cent at two examinations. Spraying was done from July 1943 on the 2—1—2 spacing

2 2

until the onset of cooler weather in mid-October, when it was changed to 3—3, as the first spacing

4

will not fit with a 72-hour digestion cycle. Results for six months have been:

Reduction in density 6 : 1. Here again the infection rate of insects escaping the spray is the same as in the untreated huts. Reduction of density alone brings about control.

As a measure of the infection potential which the spray measures had to combat, the blood of 23 persons, all of local origin, who had been living here uninterruptedly since the inception of control, commenced by anti-larval *cum* spraying in 1939, was re-examined in July 1943. A parasite rate of 56 per cent in August 1939 had been reduced to only 39 per cent in 1943.

The results of the various control measures tried at this station are as under. Railway staff, July to December incidence:

1933-1935. Average. No control .. 84 per cent.

1939 .. .. Larval and spray 48 " control.

1940-1942. Average. 7 days spraying 27 "

1943 .. .. 2—1—2 spraying 29 " 2 2 \*

\* When spaced spraying was introduced it was done also in a few aboriginal huts adjacent to the station, not sprayed in previous years.

Two points emerge from these figures: (1) At *Gua* 26 sprayings a month produce an incidence of 11 per cent for the six months covering the transmission season. At *Posoita* 15 sprayings a month produce an incidence of only 2 per cent more than can be achieved by 7-day spraying, which is probably not significant, as a single

TABLE II  
*Posoita*. *A. fluviatilis*-group daily catches and dissection

1943	UNSPRAYED			SPRAYED			DENSITY PER ROOM PER DAY		Relative* danger of month
	Number	Oöcyst rate	Sporozoite rate	Number	Oöcyst rate	Sporozoite rate	Un- sprayed	Sprayed	
July .. ..	12	0.0	0.0	7	0.0	0.0	0.03	0.01	0.0
August .. ..	7	0.0	0.0	5	0.0	0.0	0.03	0.01	0.0
September ..	11	0.0	9.1	20	5.0	5.0	0.05	0.02	1.0
October .. ..	542	5.0	2.8	387	6.5	3.1	2.19	0.42	13.5
November ..	1,325	1.9	1.4	550	2.4	0.9	5.71	0.61	17.6
December ..	865	1.2	0.2	488	0.8	0.4	3.49	0.53	1.5
Totals and average ..	2,762	2.3	1.3	1,457	2.9	1.4	1.62	0.27	

\* This figure is obtained by multiplying density by sporozoite rate. The figures so obtained are multiplied by an arbitrary factor to raise the least dangerous month to unity. Natural data (unsprayed) are used.

group of aboriginal huts about half-a-mile distant. The spleen rate of the few children year's figure is being compared with a three-year average.

(2) Comparing the two stations, under six-day spraying the reduction in density is four times as great as under the 2—1—2 spacing.

2 2

But actually the two stations are not strictly comparable. At Posoita the comparison huts in table II are almost beyond normal flight range from the railway colony and the few surrounding huts. Therefore the whole mosquito population affecting the latter is under attack when it feeds. At Gua the railway colony is surrounded by blocks of mines quarters, unsprayed, and is subject to infiltration from the undisturbed anopheline population of the mines quarters, and it appears strange that there is not more of this.

The explanation is possibly to be found in the results of a further experiment carried out by us. This has shown that if daily spraying with kerosene only is done, there is a reduction in numbers caught greater than with daily spraying with pyrethrum-kerosene mixture. This reduction can only be a repellent and not a lethal effect. But whether it is a repellence to entering to bite or only to remaining to rest after biting is not yet clear. In the first case it is advantageous, in the second the reverse, as tending to drive insects immediately after feeding beyond reach of the spray. The point is still under investigation. But we think that it is clear that repellence alone can explain why, in the case of a set of buildings surrounded by others unsprayed, there is so little infiltration. We have not so far fully studied whether the repellent effect can be obtained by spaced spraying; what evidence we have is to the contrary. But in the present pyrethrum shortage, advantage might be taken of this repellent effect by using spaced spraying, even when there is a village too large to spray adjacent, and doing kerosene only spraying on the interval days.

In camp siting, it is the invariable rule to locate as far as possible away from the nearest gametocyte-harboursing village, and therefore, as shown in the case of Posoita above, spaced spraying presents great opportunities of economy both of insecticide and effort.

Where data on seasonal intensity of infection exist, the last column in table II shows that in the months of most intense transmission it may be advisable to increase intensity of spraying temporarily, even up to daily, to obtain the theoretical maximum of hits.

In conclusion we would emphasize that the procedure here described is applicable only to the control of the *fluviatilis*-group, and not to any other of the malaria vectors of India. Russell and Knipe (1940) have shown that control of *culicifacies* is adequately achieved by once, or at most bi-weekly, spraying, though they do not state the spacing of the latter. Our unpublished work has revealed the reasons underlying this. Our observations quoted in the appendix to Covell and Singh (1942) mention

that not even daily spraying is effective against *sundaicus* when this is heavily infiltrating from distant breeding places. No data of any kind exist in regard to *philippinensis*, *annularis*, *stephensi* and any other vector.

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### INVESTIGATION ON UNDULANT FEVER IN THE CITY OF BOMBAY

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UNDULANT FEVER is generally believed to have a world-wide distribution. Surgeon Captain Hughes (1897) put forward evidence as to the possibility of the existence of this disease in China and India also. Cruickshank and Barbour (1931) have quoted Kristen saying that 'there is no reason to believe that this infection is more widespread in Denmark than in other countries where cattle breeding is carried to the same extent'. Dalrymple-Champneys (1933) presiding over the discussion on 'Undulant fever in England' before the Royal Society concluded with a plea, 'that all Widal sera should be tested against the brucella group of organisms as well as that of the members of the enteric group'. Wade (1933) succeeded in detecting four cases of undulant fever in England by routine examination of Widal sera. Mallick and Ahuja (1931) did not succeed in detecting any cases of this disease by routine examination of Wassermann and Widal sera, but they are of opinion that brucellosis may account for a considerable amount of illness in an agricultural country like India. Pandalai and Raman (1941) have reported six cases of this disease in Vizagapatam where the clinical diagnosis was confirmed by agglutination and cultural methods. Bardhan (1943) has reported thirteen cases collected by the late Captain Rajan in Lahore diagnosed by agglutination method.

As to its incidence in Bombay no data are available. The annual reports on the Civil Hospitals and Dispensaries in Bombay Province for the last ten years (1932-42) do not record



any cases under a separate heading, but show a large number of cases under the heading 'Undiagnosed pyrexial cases'. The annual reports of this Institute for the last ten years (1932-42) show that forty-five sera from clinically suspected cases were examined by the agglutination test only, and three were reported positive. The records of Widal tests of this Institute show a large number of sera which were repeatedly negative. It was thought that many of the 'Undiagnosed pyrexial cases' might be due to this disease, and therefore it was decided to investigate the incidence of this disease in the city of Bombay by examining all Widal negative sera and all Wassermann sera for evidence of this infection by means of the agglutination test. Resort was made to cultural methods where possible and advisable, as judged by the results of the agglutination test.

#### The agglutination test

Castaneda *et al.* (1942) found the agglutination test the most sensitive for the detection of

according to the methods of Lynch and Callan (1930) and, finally, homogeneous suspensions were pooled and preserved at  $\pm 5^{\circ}\text{C}$ . The final suspension of each of *Br. melitensis* and *Br. abortus* contained about 6,700 million organisms per c.cm. (opacity adjusted to no. 9 of Macfarlane nephelometer).

For agglutination, Dryer's technique was employed. The serum dilutions were made in 5 per cent saline to control zone phenomenon [Taylor *et al.* (1938)] and to 1 c.cm. of the different dilutions 0.05 c.cm. of concentrated suspension was added. The tube racks were then treated in a water-bath at  $55^{\circ}\text{C}$ . for four hours and subsequently kept in a refrigerator overnight at  $\pm 5^{\circ}\text{C}$ . The readings were recorded after twenty-four hours at ++, +,  $\pm$ , and -, according to the degree of agglutination as complete, partial, doubtful and negative respectively.

#### Results

The results are tabulated below :—

TABLE I  
Agglutinins against brucella in Wassermann and Widal negative sera

Agglutination titres	WASSERMANN SERA				WIDAL NEGATIVE SERA			
	<i>Br. melitensis</i>		<i>Br. abortus</i>		<i>Br. melitensis</i>		<i>Br. abortus</i>	
	Number	Per cent	Number	Per cent	Number	Per cent	Number	Per cent
Negative ..	1,934	92.9	1,985	95.35	232	91.0	244	95.7
Positive 1 : 20 ..	104	4.99	75	3.6	16	6.27	8	3.13
" 1 : 50 ..	36	1.73	22	1.05	4	1.56	1	0.39
" 1 : 100 ..	8	0.37	0	0.0	2	0.78	2	0.78
" 1 : 200 ..	0	0.0	0	0.0	0	0.0	0	0.0
" 1 : 2500 ..	0	0.0	0	0.0	1	0.39	1 (1 in 2000)	0.39
TOTAL ..	2,082	100.0	2,082	100.0	255	100.0	255	100.0

brucellosis. del Vecchio (1938) recommends the use of a polyvalent antigen in the diagnostic agglutination suspension, with more than two strains, as he has observed that a strain of brucella which is agglutinated by some sera is occasionally not agglutinated by human or animal serum which agglutinates other strains.

As the nature and source of infection was unknown it was decided to examine all sera by agglutination test against *Br. melitensis* and *Br. abortus*. The diagnostic agglutination suspensions were prepared from three strains of each of *Br. melitensis* and *Br. abortus*. All the six strains were obtained from the Central Research Institute, Kasauli, and all of them were found to be smooth strains, as the thermo-agglutination test at  $95^{\circ}\text{C}$ . and salt agglutination test at  $55^{\circ}\text{C}$ . were negative (Pandit and Wilson, 1932). The antigenic suspension from each was prepared, tested and standardized

#### Comment

There seems to be no general agreement as to the exact titre of the agglutination test which should be taken as diagnostic of infection. Topley and Wilson (1936) after surveying the literature are of the opinion that agglutination even in a titre of only 1 : 20 against *Br. abortus* is diagnostic of latent infection because very rarely are agglutinins found even in that titre in the sera of those persons who are not exposed to contact with infected animals and who do not drink raw milk or cream.

Our results show that the percentage of sera agglutinating *Br. melitensis* is higher than that of sera agglutinating *Br. abortus*, because it was noticed that the same serum which agglutinated *Br. melitensis* also agglutinated *Br. abortus*, but sometimes in a lower titre. Results in Wassermann sera in England and Germany show that 1.5 per cent agglutinate *Br. abortus* to

a titre of 1 : 40 or over. Our own results with Wassermann and Widal sera show an almost similar percentage with *Br. melitensis*. If this is taken as an index of latent infection due to *Br. melitensis*, then the results are rather puzzling when it is remembered that the custom of drinking raw goat's milk is uncommon in Bombay, unless it is presumed that the cows and buffaloes are infected with *Br. melitensis* or that the milk is adulterated with infected goat's milk.

#### Blood culture

The medium used for blood culture was sterile nutrient heart broth distributed in 100 c.cm. flat bottom flasks. Twenty c.cm. of blood was directly inoculated aseptically in the medium, and the partial CO<sub>2</sub> pressure required for the growth was obtained by plugging the flasks with burning cotton-wool plugs (Wilson, 1930). The flasks were incubated at 37°C. and subcultures were made every week on solid media containing 3 per cent glycerine and 1 per cent glucose agar. The flasks were discarded if the 4th subculture also showed no growth. For identification of the strains, isolated selective media containing thionin and fuchsin were prepared according to the methods of Meyer and Zobell (1932).

In five cases blood cultures were done. In two because the agglutination titre was 1 : 100 or above and in the remaining three because the clinicians so desired, even though the agglutination test was negative. In other cases where the agglutination titre was suggestive of infection, the patients could not be traced in different hospitals as most of them had been discharged. The results are given in table II.

TABLE II

Results of blood culture compared with the agglutination titre

Case number	AGGLUTINATION TITRE		Subculture on 3 per cent glycerine, 1 per cent glucose agar
	<i>Br. melitensis</i>	<i>Br. abortus</i>	
1	Positive 1 : 100	Positive 1 : 100	Growth appeared in the 4th weekly subculture.
2	Positive 1 : 2500	Positive 1 : 2000	Growth appeared in the 1st weekly subculture.
3	Negative	Negative	No growth in the 4th weekly subculture.
4	"	"	Do.
5	"	"	Do.

All these specific tests show that the two strains isolated were *Br. melitensis*. Thermo-agglutination and salt agglutination tests were negative, which showed that the strains were of smooth variety. The pathogenicity of these

TABLE III

Study of two cultures isolated

Culture	MACROSCOPIC SLIDE AGGLUTINATION WITH HIGH TITRE OXFORD SERA		STUDY OF GROWTH			
	<i>Br. melitensis</i>	<i>Br. abortus</i>	CO <sub>2</sub> requirements	H <sub>2</sub> S test	Thionin medium	Fuchsin medium
1	+	+	Nil	Negative	++	++
2	+	+	Nil	"	++	++

strains for white mice was tested according to the method of Feldman and Olson (1935). Two mice for each strain were used. Each pair was given 0.25 c.cm. of an inoculum of a forty-eight hours' growth standardized to contain about 768 million organisms per c.cm. from respective strains. The mice were killed after one month. In all the four, a slight enlargement of the spleen was noticed. No other focal lesions were seen. The causative organism was isolated from splenic subcultures. No histological examination of the enlarged spleens was done.

#### Comment

Both the cases from which the *Br. melitensis* strain was isolated were being treated for enteric infection. No history of drinking raw goat's milk or history of contact with cattle and goats was obtained. No history of a similar kind of illness in their family was obtained. Both were non-residents of Bombay proper. One came from Lahore and the other from Kathiawar. Serefettin (1936) working on undulant fever in Turkey states that 'clearly infection with brucella is not widespread in Turkey and this is probably due to the custom of boiling milk before use'. It is likely that acute infection in Bombay is also uncommon due to the same custom and it is equally likely that agglutinins in low titre are due to low-grade infection by attenuated organisms of *Br. melitensis*, the attenuation being brought about by the process of boiling milk. A further study is required to explain the source of *Br. melitensis* infection.

#### Summary

1. In all, 2,082 routine Wassermann sera were examined for agglutinins against *Br. melitensis* and *Br. abortus*. The number of positive sera for *Br. melitensis* was 104 (4.995 per cent) in 1 : 20 ; 36 (1.73 per cent) in 1 : 50 ; and 8 (0.37 per cent) in 1 : 100. The number of positive sera for *Br. abortus* is 75 (3.6 per cent) in 1 : 20 ; 22 (1.05 per cent) in 1 : 50 ; and 0 (0.0 per cent) in 1 : 100. The same serum

which agglutinated *Br. melitensis* also agglutinated *Br. abortus* though sometimes to a lesser titre.

2. In all, 255 Widal negative sera were similarly examined. The number of positive sera for *Br. melitensis* was 16 (6.27 per cent) in 1 : 20 ; 4 (1.55 per cent) in 1 : 50 ; 2 (0.78 per cent) in 1 : 100 ; 1 (0.39 per cent) in 1 : 2500. The number of positive sera for *Br. abortus* was 8 (3.13 per cent) in 1 : 20 ; 1 (0.39 per cent) in 1 : 50 ; 2 (0.78 per cent) in 1 : 100 ; 1 (0.39 per cent) in 1 : 2000.

3. In five pyrexial cases blood cultures were done ; in two because the agglutination titre was 1 : 100 and above, and in the remaining three because the clinicians desired though the agglutination test was negative.

From the first two cases *Br. melitensis* was isolated.

### Conclusion

Acute infection with brucella organisms is uncommon in Bombay and this is probably due to the custom of boiling milk before use.

### Acknowledgment

I am very thankful to Dr. Soman for his valuable guidance throughout.

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## A PRELIMINARY NOTE ON THE PREPARATION OF ANTI-Rh AGGLUTININ

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THE test serum for detecting the Rh antigen in the red cells of the human population may be prepared according to the technique originally described by Landsteiner and Weiner (1941) by the injection of red cells from the Rhesus monkey into guinea-pigs or rabbits. As in other immunological experiments, only a few of the animals thus treated yield a satisfactory anti-serum. Even then, the action of such a serum is complicated by the presence of group-agglutinins which in an undiluted state generally agglutinate human red cells of all groups. To eliminate the false positive reactions, serum thus prepared is diluted with normal saline. The amount of dilution required to eliminate false positive reactions is variable, so that each batch of serum has to be standardized against a known standard.

Sera of mothers giving birth to children suffering from erythroblastosis-fœtalis are, in many cases, good sources of potent anti-Rh agglutinins, and serve as standards for the test serum prepared by immunizing rabbits or guinea-pigs.

For reasons not fully understood, very few cases of erythroblastosis-fœtalis are reported here in India, and so far maternal serum of such cases has not been available. While thinking of some means of obtaining the test serum from the animals in a more purified form, I wondered if purified anti-Rh agglutinins could be obtained by employing the technique described by Landsteiner and Miller (1925), for obtaining purified anti-A and anti-B agglutinins. Experiments were, therefore, undertaken to find out if purified anti-Rh agglutinin could be prepared in the same way, by first producing anti-Rh agglutinin in a susceptible animal by injection of red cells from a rhesus monkey, later absorbing the anti-Rh agglutinin with cells, and finally dissociating the agglutinin from the cells at a higher temperature.

**Method.**—Washed red cells of rhesus monkeys were repeatedly injected into eight rabbits, two of which died during the course of injections. From the six surviving rabbits, 15 to 20 c.cm. of blood was collected by heart puncture ten days after the last injection.

The undiluted serum from all these animals strongly agglutinated the human red cells of all groups. With diluted sera, agglutination was seen up to a dilution of 1 in 80 in one, 1 in 60 in another, and 1 in 40 in the remaining four animals.

To a small quantity of serum from each animal were added some washed red cells from a rhesus monkey, and the mixture was kept for three to four hours in a 15°C. incubator. At the end of that time, the supernatant fluid was discarded

TABLE

GROUP AB			GROUP A			GROUP B.			GROUP O		
Number tested	Number positive	Number negative	Number tested	Number positive	Number negative	Number tested	Number positive	Number negative	Number tested	Number positive	Number negative
22	21	1	65	57	8	74	70	4	79	68	11

and a little saline was added to the red cells. The mixture was kept at 56°C. for 5 minutes to dissociate the agglutinin from the red cells, the fluid was separated while still hot, and the tests were carried out with the fluid thus prepared.

**Results.**—Clear-cut positive and negative results were obtained with the fluid prepared as above from the serum of those two rabbits whose untreated serum also showed clear-cut agglutinations with most cells in high dilution, 1 in 60 or more; so far 240 samples of blood of different groups have been tested with the fluid thus prepared; the incidence of the positive and negative results in these samples were as follows :—

Total number tested .. 240  
 Total number positive .. 216=90 per cent  
 Total number negative .. 24=10 „ „

Analysing the results according to the ABO blood groups, the incidence of Rh positive and Rh negative bloods in the different blood groups is shown in the table above.

Over 70 per cent of the samples of blood which were examined with the prepared test fluid were also examined with untreated but diluted sera from the same two rabbits, to compare the results between the two methods. It was seen that Rh positive cases, as determined by the prepared test fluid, always showed clear-cut agglutination with the untreated diluted serum in a dilution of 1 in 60, and in about 50 per cent of the cases even in a dilution of 1 in 80; but in the Rh negative cases, determined by the prepared test fluid, clear-cut agglutination though always seen with untreated diluted serum in a dilution of 1 in 20 and sometimes even in 1 in 40 was never seen in any dilution higher than that.

In the absence of any standard serum with which the results obtained by the two methods could be compared, the results obtained with the prepared test fluid appear to be much better than those obtained with the untreated serum. The action of the prepared fluid in detecting the Rh agglutinin of the human red cells appears to be specific. Further work is in progress to confirm this.

**Conclusion.**—From the results obtained, it is reasonable to conclude that the anti-Rh agglutinin contained in the test fluid prepared by the method described above is obtained in a purified form, as it clearly differentiated between the Rh positive and Rh negative cases in the 240 samples of blood tested so far.

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## A STUDY OF 10,000 DELIVERIES

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THIS investigation has been undertaken with a view to making a study of the statistics of 10,000 deliveries in this hospital compared with similar statistics published in the *Indian Medical Gazette* and standard textbooks. For the purpose of this analysis the case-sheets of 10,000 parturient women with viable infants have been selected. As many of the women were uncertain of the date of the last menstrual period, and as the height of the uterus at the 28th week is variable, the case-sheets of those women who gave birth to infants of less than 4 lb. in weight have been excluded, and multiple pregnancies omitted. Only the main denomination in compound presentations is mentioned.

TABLE I

Particulars	Percentage in 10,000 deliveries	Percentage given in 2,500 full-term primiparae	Percentage given by Holland	Percentage given by Green-Armytage	Percentage given by Mudaliar
Vertex ..	96.3	97.64	96.0	96.0	..
Face ..	0.53	0.16	0.33	0.4	0.4
Brow ..	0.05	Nil	0.06 to 0.05	0.06	0.04
Breech ..	2.32	1.96	3.3 to 1.6 average	5.0	2.4
Transverse ..	0.75	0.24	0.5	1.0	0.6

A study of the statistics given above shows that the proportion of the various presentations is more or less the same in any given series of deliveries. It is also noteworthy that in primiparae series presentations other than vertex are less common than in general series.

Table II shows that forceps deliveries are more common in primiparae although normal vertex presentations are the rule. This may be accounted for by the element of fear and want of training for child-birth. Brown says aptly and succinctly that fear produces tension; tension, pain; and pain increased fear. He also says that a tense woman means a tense cervix and a tense cervix means a prolonged, painful and difficult labour.

TABLE II

Comparative statement showing the percentage in the methods of delivery

	Percentage in 10,000 series	Percentage in 2,500 full-term primiparae series
Normal .. ..	94.64	90.95
Forceps .. ..	3.98	8.2
Internal podalic version ..	1.11	0.4
Cæsarean section ..	0.27	0.44

TABLE III

Comparative statement regarding ratio of sex of child

Particulars	In 10,000 series	In 2,500 series
Boys ..	526.5	522
Girls ..	473.5	478

This table confirms the fact that the incidence of male and female births is approximately equal. Sex is a Mendelian character of heredity and the two possible combinations resulting in males and females occur in equal numbers—where large numbers of matings are involved. A very interesting chapter on this subject is given in Professor F. J. Brown's book, 'The Antenatal and Postnatal Care'.

TABLE IV

Maternal and neonatal mortality per thousand

Particulars	In 10,000 series	In 2,500 series
Maternal ..	9.0	7.6
Neonatal ..	54.5	43.0

The incidence of maternal and neonatal mortality is greater in the mixed series than in the 2,500 primiparae series. It is due to abnormal presentations and increased incidence of diseases in multiparae.

TABLE V

Average weight of new-born infant

In 10,000 series	.. 6 lb. and 6 oz.
In 2,500 series	.. 6 lb. and 2 oz.

This confirms the popular belief that in multiparae the baby is heavier at birth than in primiparae.

#### Conclusions

1. Abnormal presentations are definitely less in primiparae, while forceps deliveries are more common.
2. The proportion of male and female births is approximately the same where large numbers of matings are involved.
3. The weight of the new-born baby is greater in multiparae.
4. The maternal and neonatal mortality rates are higher in the 10,000 series, though the percentage of abnormal deliveries is more in the primiparae series.

We are grateful to Colonel J. C. Pyper, O.B.E., I.M.S., for his helpful suggestions, and to Dr. Ramgopal and Sister L. D'Souza, for helping us with the statistics.

## A Mirror of Hospital Practice

### SULPHANILAMIDE IN A CASE OF ABDOMINAL INJURY

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The following case appears worthy of record :—

L. D. was gored by a wild boar at night in his field while watching his crops on the 10th March, 1944. After a lapse of twenty-four hours he was carried to the dispensary, a distance of ten miles over and down the ghats. He had irregular contused wounds of the back muscles and several gashes on the right abdominal wall and thigh. The peritoneum was ripped open about two inches on the outer border of the rectus and a large mass of omentum and one-and-a-half feet of small intestine had prolapsed. He was suffering from shock, and appeared moribund. The whole mass had been covered with ashes, turmeric powder and a paste made of green jungle-leaves, and tied up with dirty rags and old 'pugree'. Under a morphia injection the skin, wounds and bowels were repeatedly cleaned with boiled water and all foreign bodies were wiped out. The bowels were not punctured. The raw surfaces including the mesentery folds were covered with boiled towels, cleaned with ether, and dusted with sulphanilamide, two-and-a-half grammes (Evan's streptocide). Under procaine locally, the prolapsed parts were gradually replaced, and the abdominal opening closed in layers with a drainage tube. Anti-tetanic serum was given. Also streptocide solution 2½ per cent 5 c.cm. intramuscularly, saline with adrenalin by rectal drip, and glucose by mouth were given. One gramme of streptocide powder was given at bed time, the temperature being 100°F., pulse 160. Next day the

temperature was 100°F., and the pulse 140. Enema given, and rectal saline continued. Streptocide 0.5 gm. given every eighth hour; flatus tube passed with some relief. On the third day the temperature was 98.5°F., and the pulse 120; streptocide continued. The patient was very restless with acute distension of abdomen. Pituitary extract 1 c.cm. given by injection, castor oil 1-oz., and turpentine stupes externally relieved the distension. On the fourth day, the temperature and the pulse became normal. Streptocide was continued till the eighth day and then stopped. The main abdominal wound appeared to heal by first intention, but the damaged skin tags and tissues gave way in some places and caused a gaping raw surface. On the thirteenth day these surfaces were brought together and sutured, and where this was not possible, skin-grafting was done which took well. After over a month in the hospital he was discharged.

My thanks are due to the authorities of the Andhra Valley Power Supply Company for permission to publish these notes.

### MALARIA IN THE NEW-BORN

By B. M. ADHICARY, L.M.F., L.T.M.  
Challapore Tea Estates

AN infant just 15 days old started a continued pyrexia on the 10th June, 1943. A peripheral blood film was taken on the 12th and was sent down to the Central Laboratory at Madabpur for examination. M.T. rings were found in the film (heavy infection). The infant was put on to quinine orally and made an uninterrupted recovery.

#### ERRATUM

The last word 'eruptions' in paragraph 2, page 251 (left-hand column) of the article on 'Influence of milk powder on fluorine intoxication in rats', published in the June number should read as 'injections'.

# HIGHLY POTENT WHOLE LIVER EXTRACT

HG % RBC count

100	5
90	4.5
80	4
70	3.5
60	
50	
40	
30	



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## Indian Medical Gazette

AUGUST

### PRIMARY ATYPICAL PNEUMONIA

IN recent years many cases of an acute respiratory infection associated with peculiar pulmonary lesions have occurred in America, England and continental Europe, sometimes assuming epidemic proportions particularly in military camps. The clinical picture is not quite new; for a decade we have known it under various names such as pneumonitis, but it is now being called atypical or virus pneumonia, a name which, though not satisfactory, must continue, we suppose, until its aetiology is cleared up. It has practically nothing in common with the classical pneumonias we have known. The signs and symptoms may vary from individual to individual and are too indefinite to make a clear-cut picture possible, the outstanding features being the paucity of physical signs in the chest when compared with x-ray findings.

The incubation period varies from one to three weeks, and the onset is insidious, with chills, malaise and muscular aching or with 'cold in the chest'. The most common early symptom is a dry cough which later becomes productive and often paroxysmal. Usually there is pain in the chest of an aching character, or a soreness behind the sternum, but pleuritic pain, dyspnoea and cyanosis are not common. There is a moderate rise of temperature which is of remittent or intermittent type, although afebrile cases have been described. The temperature falls by lysis in about 10 days, but it may last much longer. The rate of respiration is not accelerated. Physical signs in the chest are few or absent especially in the early stage, but one significant and perhaps the only abnormal and localizing sign is that the breath sounds are suppressed over the involved areas, and with it there may be a few râles at the end of inspiration, particularly after coughing. Complications and sequelae are rare.

Blood culture is sterile, and the white cell count is normal or slightly raised, with perhaps a relative increase of mononuclear cells. No predominating pathogenic organisms are found in the sputum.

The diagnosis rests mainly on x-rays, but x-ray findings are variable. A radiogram shows patchy opacities; the lesions are more often found in the right lung, especially in the lower lobe, but may be bilateral. In a series of 50 cases, Drew and his colleagues (1943) found two

types, viz (1) a woolly area of indefinite outline, less dense and more mottled than in pneumococcal pneumonia and (2) an area, radiating from the hilar shadow which is enlarged in the great majority of cases, this area showing reticulation. One distinctive feature of the x-ray appearances is their shifting nature; they may appear and disappear overnight. No relationship is, however, observed between the extent of the radiographic lesion and the severity of the symptoms. The woolly mottling, when it occurs in the upper lobe, may be confused with pulmonary tuberculosis, and, on erroneous diagnosis, patients have been sent to sanatoria, and soldiers discharged from the army.

The disease tends to occur sporadically, but sometimes in epidemics, and is thought to spread from patient to patient, but, in general, susceptibility to infection is perhaps low. Prolonged contact as in barracks may however result in a high incidence. The majority of cases have occurred among young adults. The disease usually runs a benign course, but there have been some outbreaks in which the infection was severe and deaths have occurred. Thus at San Francisco in 1940, a patient was admitted into hospital and died; three nurses who looked after him took the infection and died; three doctors in the pathology department who examined the organs of the fatal cases also contracted a severe infection, recovery being very prolonged (Brown *et al.*, 1943).

The essential pathological lesion is an interstitial broncho-pneumonia and a concomitant bronchitis with collapse of adjoining areas of the lung. Attempts to find the causative agent have so far failed. It does not appear to be a bacterium; there is no leucocytosis, and the disease does not respond to sulphonamide therapy. (The last characteristic, incidentally, was the chief thing to raise suspicion that this was a disease previously unrecognized; and is still one of the criteria on which diagnosis of atypical pneumonia is made.) On the other hand the resemblance of the lung lesions to those of certain virus and rickettsial diseases suggests a similar aetiology. For instance, the virus of influenza, psittacosis and lympho-granuloma and the rickettsia of Q fever are known to cause an atypical form of pneumonia.

Is it a new disease or a recrudescence of a disease which has remained quiet for a long time, or has it been always with us but not recognized? The general opinion is that the syndrome has occurred in the past, and its common recognition now is due to more frequent use of x-rays for diagnostic purposes. Indeed its incidence may be much higher than is generally appreciated. Some say that the 1918 influenza epidemic included cases of atypical pneumonia; others do not agree. Physicians in India may be able to recall cases in their practice which in retrospect might have been cases of atypical pneumonia. In 1942 Napier, Chaudhuri and Rai Chaudhuri reported a case

of this kind in our columns, diagnosed as 'pneumonitis'. It is well to be on the alert as the disease seems to be increasing in frequency.

R. N. C.

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### INTESTINAL FLORA AND VITAMIN B<sub>1</sub>

REGARDING vitamin B<sub>1</sub>, Bicknell and Prescott in their recent standard book on the subject of vitamins make the following statement:—

'Man is unable to synthesize vitamin B<sub>1</sub> nor can he store it to any appreciable extent. It is readily absorbed from both the small and perhaps the large intestine, although the work of Schroeder and Liebig, who administered the vitamin to patients through a cæcostomy, suggests that it is not absorbed from the large intestine.'

A paper recently appeared in the *Journal of the American Medical Association* written by Najjar and Holt in which the accuracy of these ideas is challenged. This article of Najjar and Holt is reprinted in our present issue page 393. Also in our present issue we publish a letter from a correspondent which bears on this matter.

Najjar and Holt working in America took up adolescent male adults living a sedentary life and placed them on an artificial diet containing a known amount of thiamin. To begin with 1 mgm. of thiamin per day was given. Careful physical examinations were made regularly for evidence of deficiency and the thiamin excretion in the urine was followed daily. The experiment was continued for 18 months and the intake of thiamin was gradually reduced during this period. When the intake was reduced to about  $\frac{1}{2}$  mgm. per day, the urine excretion became very small but still measurable by special methods. With further reduction in the thiamin intake, this small urine excretion still persisted. After several months on a thiamin intake between 0.1 and 0.2 mgm., no sign of deficiency appeared. When the thiamin intake was reduced to nil, symptoms of deficiency took several weeks to appear and even then were seen in only 5 out of the 9 subjects.

In investigating this question it was found that in the stools of the remaining 4, considerable quantities of free thiamin was found, while, in the 5 with symptoms of vitamin deficiency, free thiamin was almost absent. The paper of Najjar and Holt gives various reasons for

believing that the thiamin in the faeces was being synthesized by bacterial action, and was not excreted from any reserve in the body. In order to obtain direct evidence on this point one of the patients was given succinyl sulphathiazol by mouth 1.5 gm. every 4 hours for one week. The thiamin excretion in the faeces stopped and reappeared a few days later after the drug had been discontinued. It thus appears that thiamin was being produced by bacterial action in the gut, but even so it had still to be shown that thiamin could be absorbed from the large intestine, for this is against the generally accepted view. Enemas containing thiamin were given in 2 persons and produced a marked rise in the urinary thiamin, thus showing that thiamin could be absorbed from the large intestine.

Thus, the work of Najjar and Holt was in many ways against the accepted views on this subject. If these findings are confirmed, then the bearings on present theory and practice are numerous and important. As Najjar and Holt say, it is likely that the biosynthesis of thiamin is greatly affected by diet, as it is known to be in animals, and, if so, we must think in terms of thiamin requirements on particular diets rather than of requirement in general. These authors also suggest that these findings may have a bearing on some of the anomalous and unexplained facts about beriberi.

Beriberi has a peculiar distribution. It is common in China, Siam, Malaya, etc., and rare in India. It used to be said that the distribution of beriberi was explained by the fact that the people in the areas in which it occurred ate only polished rice but the inadequacy of this explanation has long been apparent. In India many people eat only polished rice but very few develop beriberi. It may be that even on a polished rice diet beriberi will not develop unless the rest of the diet is such as not to facilitate the biosynthesis of thiamin in the gut.

One point arising out of this work is obvious. If the people's diet is inadequate, if they depend to any considerable extent on the synthesis of thiamin in the gut for meeting their thiamin requirements, and if this synthesis depends on bacterial action which is prevented by the administration of drugs, such as the sulpha group of drugs, which markedly reduce bacterial activity in the gut, it seems possible that the symptoms of thiamin deficiency may be induced by the administration of these drugs. This will mean that in any patient under treatment with these or similar drugs, great care must be exercised to see that the vitamin in the diet is adequate in amount so that the loss of the biosynthesis will not be detrimental.

All this is speculative. It does appear however that an interesting line of investigation has been opened up, and that the study of the intestinal flora in relation to nutrition may give interesting results.

## Special Article

### CARDIO-VASCULAR SYPHILIS\*

By U. P. BASU, M.B., F.R.C.P.I., F.S.M.F.  
Principal, Medical College, Calcutta

CARDIO-VASCULAR syphilis presents important, interesting and difficult problems which are engaging the anxious consideration of cardiologists and the syphilologists. Its importance can be realized from the confession of the modern Hippocrates, Sir William Osler, who in his early life regarded syphilis as the third in the list of deadly diseases which takes the largest toll of human lives; but in his later years he changed his opinion in the light of further information obtained regarding the havoc caused by cardio-vascular syphilis and thought that syphilis outranked even tuberculosis and was the greatest cause of human death. His reference obviously was to the incidence of syphilis in the West.

I tested the Wassermann reaction of all the patients who were admitted in my wards in the Medical College Hospitals, Calcutta, during the year 1931, and found the reaction to be moderately and strongly positive in 1 per cent of the patients. It must, however, be remembered that, in the diagnosis of syphilis, the blood Wassermann reaction may present all grades of fluctuations; from complete and persistent negative to complete and fixed positive. It is likely, therefore, that this small incidence of luetic infection in my patients could not be taken at its face value.

Syphilis vies with its sister disease tuberculosis in affecting any tissue of an infected individual, and it out-distances the latter in its power to transmit the germ to successive generations. The chief cause of death in a syphilitic is cardio-vascular involvement.

It has been held that nearly 33 per cent of all fatal cases of syphilis belongs to the cardio-vascular type. In 23,000 autopsies in a General Clinic, Langer (1926) found that 70 to 80 per cent of syphilitic patients had cardio-vascular syphilis. Warthin in 1916 substantiated vascular lesions by microscopical examinations in over 85 per cent of syphilitic patients. Cardio-vascular syphilis is three times more frequent in males than in females.

In the year 1927 I found among a total number of 400 cardio-vascular cases treated in the Calcutta Medical College Hospitals, rheumatic infection could account for 168 cases and syphilitic infection for 20 cases (Basu, 1928). Much water has flown through the Bhagirathi since that time, and although I cannot state definitely the incidence of syphilis to-day, I feel

no hesitation in saying that the disease has increased markedly during the last decade. The total number of cases of syphilis treated in the hospitals of Bengal according to the Surgeon-General's report has increased from 12,605 in 1937 to 15,539 in 1941. Seeing that detectable clinical cardio-vascular manifestations do not take place for 10 to 15 years after the infection, we may reasonably expect to find a large number of cases in the course of next few years. The interesting feature of syphilis is that, if thoroughly treated on its first manifestation, the untoward developments of tertiary lesions could be wholly prevented. The difficult problem in the subject is the management of a full-fledged cardio-aortic syphilis with its dread Jarisch-Herxheimer reaction.

Broadly speaking, a clinical study of syphilis of the heart resolves itself into a consideration of the symptoms dependant upon aortitis, aortic aneurysm, coronary disease, aortic regurgitation and myocarditis. It is probable that all these conditions co-exist when the disease has got a firm hold in the heart and aorta.

It is during the septicæmic stage of syphilis that *Treponema pallidum* attacks the heart, but the infection remains latent till the symptoms of aortitis become evident. Actually a case has been recorded where a patient died of syphilitic disease of the coronary artery and autopsy confirmed the clinical diagnosis although the patient had chancre only two years before (Maynard *et al.*, 1935). The bulb and lower portion of the ascending aorta are invaded through the vasa vasorum from peri-aortitis and mediastinitis attendant upon syphilitic involvement of, and spread from, the neighbouring lymph nodes. It travels through the peri-vascular lymphatics and goes to the media which is the vital part of the aorta, and produces replacement fibrosis. There is no doubt that quite a good number of cases resist the aortic infection for some time, probably because the spirochaetes fail to enter the vasa vasorum. Again, we should not lose sight of the fact that in such cases the syphilitic toxin may cause arterial contraction and raise the basic diastolic pressure which compresses the openings of the vasa vasorum (Stephens, 1932). In this matter of latency in the manifestation of cardio-vascular symptoms, chronic syphilitic infection resembles the sister protozoal disease, chronic amoebiasis, in its late manifestations of hepatitis and liver abscess. The aortic valves are affected in a dual fashion. The infection of the aorta may give rise to generalized dilatation or localized aneurysm, weakening of the aortic ring and incompetence of the flaps of the aortic valves, but the infection may spread to the mouth of the coronary artery and to the aortic valves themselves which show fibrosis, ultimately leading to scarring and puckering. It must be remembered that the lumen of the coronary arteries remains unaffected, that syphilitic aortic stenosis is a very rare sequela in the process of infection, and that

\*Being an address delivered to the Post-graduate Training Course (Anti-Venereal Disease Campaign sponsored by the Government of Bengal).

syphilitic mitral valvular disease is unknown. When both the lesions co-exist, namely, coronary embarrassment and a leaking aortic valve, the condition becomes serious because the heart muscle is saddled with the load of aortic reflux and, therefore, is overworked and at the same time it is getting under-nourished due to proliferation of the intima at the mouths of the coronary arteries. The heart muscle itself is affected by syphilis in very many ways. Thus there may be diffuse interstitial infiltration, disintegration and absorption of multiple gummas, or there may be degenerative changes near the terminals of the coronary arterioles, or the muscle may show degeneration and replacement following obstruction of the minute coronary vessels.

Syphilitic aortitis can be recognized much earlier than it has been in the past. In order to discover its presence early, one should pay heed to such subjective symptoms as substernal pain in a patient in middle life, paroxysmal attacks of dyspnoea, increased pulsation in the supra-sternal notch, increase in the area of supra-cardiac dullness and a tympanitic quality of the aortic second sound in the absence of hypertensive heart disease. Dilatation of the aorta usually produces dullness behind the sternum at the level of the second, and often up to the first interspace. The borders of such dullness may extend  $\frac{1}{2}$  inch to the left and a little more to the right of the sternal borders. This area on percussion rarely exceeds  $2\frac{1}{2}$  inches (6 cm.) in diameter in simple dilatation. The tympanitic nature of the aortic second sound can be well mimicked by holding a strip of linen between the two hands and suddenly stretching it. When these visible signs and symptoms are present, an attempt should be made to elicit the previous history of syphilis, unless it is a case of proved syphilis. The physician here will encounter some difficulty, as it is a curious fact that the psychology of the followers of Venus is fundamentally different from that of Bacchus. Whereas the former will show the typical truculent behaviour of a neuro-mimetic, hiding the history of syphilitic infection as best as he can, the latter exhibits the characteristic *bonhomie* of an alcoholic and gives the history of syphilis uncalled for.

But instead of depending upon the history and waiting for these symptoms to develop, it will be a wise step to examine a syphilitic patient at regular intervals after the primary infection by roentgenographic and fluoroscopic examinations in order to detect slight dilatation of the aorta. In normal persons under 50 years of age, the diameter of the ascending aorta seldom exceeds 3.5 centimeters in the antero-oblique view underneath the screen. Any dilatation beyond this limit can be easily measured by an orthodiagram or a teloradiogram. In this respect, radioscopy of the heart is more important than electrocardiography, as the condition gives no typical picture in an electrocardio-

gram. One word of caution is necessary in diagnosing syphilitic dilatation of the aorta, namely, the necessity of exclusion of hypertension, which is the other chief cause of aortic dilatation. But both may be found together, in which case differentiation is extremely difficult. As the aorta begins to dilate, a soft blowing diastolic murmur will be heard in the third or fourth interspace to the left of the sternum, often accompanied by soft systolic murmur at the base of the heart and a pulsation will appear in the right of the sternum in the second and third interspace. X-ray will show the pulsatile swelling, and palpation will establish its expansible nature. The aortic second sound will be palpated as a distinct thud.

### Case 1. A case of syphilitic aortitis

Many years ago I had in my charge a patient, a zamindar, aged 50. His chief complaint was that about 8 a.m. in the morning, about three or four times a week, he used to feel a sense of oppression over the upper part of the sternum, the moment he would alight from his carriage and walk a few steps. This embarrassing symptom used to oppress him from a few seconds to a minute or two, and as he used to ignore it and continued to walk, it would pass away. For this unpleasant symptom regularly appearing and giving him discomfort, he consulted many leading physicians of the town but no cause was detected. Ordinary examination of the heart was done but in those days radiology of the heart was seldom performed. For nearly 5 years the gentleman continued to suffer in this way till one morning the same symptom became considerably more marked, giving rise to intense acute pain at the height of which he brought out enormous quantity of fresh frothy blood and from asphyxia occurred death.

The symptom complained of by this patient, interpreted in the light of the way in which he died, leaves no room for doubt that his early symptom was due to syphilitic aortitis and the cause of his death was rupture of the aneurysm into the air passages.

When there is a frank aortic leakage, the classical signs and symptoms will be present which are so well known. Suffice it to say that 'Oppolzer won his Professorship at Vienna by casually making a diagnosis of aortic insufficiency while walking round the wards of the hospital and merely resting his hand upon the dorsum of the patient's foot and palpating the bounding and collapsing pulse due to high pulse pressure (Hirschfelder, 1918)'. Apart from anaemia and arterio-sclerosis, carotid pulsation is an outstanding sign of well-established aortic regurgitation and can be well seen in an uncovered neck from the height of one storey. This ocular diagnosis of aortic regurgitation can be confirmed by palpation of the pulse, not by the tips of the fingers but by the phalanges while holding the arm with the other hand, when the characteristic pulse first described by the great Irish physician, Sir Dominic Corrigan, can be felt like a water-hammer, that is to say, if a pulse tracing is taken, the pulse wave will show a sharp rise, a clear top and a quick drop.

The other physical signs at this stage of the disease are: marked hypertrophy of the left



out-flow tract giving rise to cor-bovinum, the diffuse heaving apical impulse, a systolic apical murmur of relative mitral insufficiency with or without a diastolic Austin-Flint murmur, a high systolic and low diastolic pressure with widening pulse pressure, a pistol-shot sound over the larger arteries of the extremities and Duroziez's sign. The cerebral symptoms of this disease and the anæmic appearance are due to the emptiness of the arterial tree.

Indeed if a differential diagnosis of aortic regurgitation is to be made, the question of anæmia should loom in one's mind larger than its sister affection, mitral disease, with its congested cheeks which at once distinguish it from aortic regurgitation. The aortic and coronary diseases are associated with pain but the latter is also associated with dyspnoea. The cause of pain is ischæmia, stretching or inflammation of nerve, or erosion of bones, and that of the dyspnoea is difficulty of transportation of blood-containing oxygen. Adequate supply of blood to the arterial walls is a matter of vital importance. If this is not ensured, degeneration sets in and the arteries lose their function of contraction and dilatation in response to nervous impulses to enable oxygen and food-containing blood to be conveyed throughout the body. Peabody and his associates have shown that basal metabolism (minimal oxygen requirement of the body at rest) is raised in patients with heart disease. When the output of the heart is inadequate to meet the requirements of the body, lactic acid accumulates in the muscles, the hydrogen-ion concentration of the blood rises, and the patient becomes dyspnoeic. When, on the other hand, it is only an isolated group of muscles that is deprived of its blood supply, the presenting symptom is not dyspnoea but pain. The sudden death in aortic regurgitation as well as in coronary disease is due to ventricular fibrillation consequent upon ischæmia following defective coronary circulation either due to blocking of the mouth of the coronary vessels mentioned above or due to a low diastolic pressure.

Whereas syphilitic aneurysm of the smaller arteries seldom occurs, aortic aneurysm is unquestionably of syphilitic origin. It is often saccular and frequently affects the ascending aorta. Large aneurysm may be present without symptoms and without interference with cardiac output. Pressure symptoms depend upon the locality affected and consist of:—

(1) Tracheal or bronchial compression giving rise to brassy cough, tracheal tugging or even pulmonary atelectasis mistaken for pneumonia.

(2) Hoarseness or aphonia from pressure on the recurrent laryngeal nerve.

(3) Inequality of pupil from pressure on cervical sympathetic.

(4) Inequality of brachial blood pressures and radial pulses. Blood pressure differences must exceed 20 mm. of mercury, to be significant.

(5) Oesophageal compression giving rise to dysphagia.

### *Case 2. Aneurysm of the descending limb of the arch of the aorta*

In October 1930, a Mohammedan sailor aged 35, who contracted syphilis 20 years ago, was admitted in my ward at the Calcutta Medical College Hospitals for the treatment of vomiting of blood, duration 5 years, and pain in the right hypochondrium and right side of the chest, one year's duration (Basu, 1933). There was also præcordial pain present every now and then which was of a dull nature. Physical examination revealed that the apex beat was in the sixth space 1 inch lateral to the mid-clavicular line. There was a feeble visible pulsation in the left first, second and third interspaces over an area about 2 inches in circumference. There was no pulsation nor any bulging on the back between the scapula and the mesial line; the cardiac impulse was heaving in character; but there was no thrill either at the apex or at the base of the heart. There was, however, a well-marked thrill over the right carotid just above the clavicle occupying the whole of the systole and continuing into the earlier part of the diastole. The left border of the heart was about 1 inch lateral to the mid-clavicular line; the upper border on the second left space and the right border merged with the lateral sternal line. In the mitral area the earlier part of the first sound was audible but the latter part replaced by a murmur which was systolic in time and was of a soft blowing nature conducted towards the axilla. The second sound in the mitral area was normal. In the pulmonary area the first sound was completely replaced by a systolic murmur louder than that heard in the mitral area. The pulmonary second sound was accentuated. In the aortic area the first sound was completely replaced by a murmur conducted along the carotids and the second sound was feeble. There was no diastolic murmur in this region. Just above the clavicle and over the right carotid, a loud systolic murmur was present. There was no pistol-shot sound; no Duroziez's murmur nor was there any systolic murmur on the back. The radial pulse rate was 92 per minute, equal on both sides, regular but collapsing. Blood pressure: right brachial systolic 110 mm. Hg. diastolic 50 mm. Hg. There was no dry or brassy cough, nor any change in the voice. The vocal folds were normal, there was tracheal tugging present but no tracheal whiff. Blood examination revealed a severe grade of secondary anæmia. The Wassermann was moderately positive. A clinical diagnosis of aneurysm of the arch of the aorta was given which was confirmed by the roentgenological examination which showed a large aneurysm of the descending limb of the arch of the aorta.

Necropsy revealed a large saccular aneurysm of the descending limb of the arch of the aorta, thickening of the aortic valves and an enlarged flabby heart.

The unusual features of this case were the abnormal pulsation in the left three interspaces in a case of aneurysm of the descending limb of the arch which usually gives rise to a bulging and a visible pulsation on the back between the scapula and the spine, the absence of dysphagia which is a common finding in such an aneurysm and the complete freedom from dyspnoea; but the behaviour of aneurysm is often very curious, and it more often pushes aside the soft structures in relation to it than it compresses them. It is surprising to come across such a large aneurysm in these days of thorough anti-syphilitic treatment, which has made aneurysms extremely uncommon. The



symptoms of hæmatemesis and right hypochondriac pain could not be correlated with the physical signs which were themselves anomalous on account of the concomitant presence of a severe grade of a secondary anaemia.

### Diagnosis

Sir James Mackenzie suggested that the senior physician should take the out-patients department, because it is at the out-door that an experienced physician has the opportunity to detect early symptoms of such diseases as pulmonary tuberculosis, syphilitic heart disease, gastric ulcer at a stage when proper attention may check further development of the disease which at a later stage produces physical signs which are difficult to remove when such patients seek admission in the wards of a hospital to be treated by an internist. In border-line cases of cardio-vascular syphilis with negative serological findings, important confirmatory evidence may be found upon a careful neurological examination including analysis of spinal fluid. Cole *et al.* (1936) have been impressed by the frequency of involvement of the central nervous system in cases of cardio-vascular syphilis. The diagnostic procedure of provocative injection is not without danger in persons suspected of having cardio-vascular syphilis, on account of the therapeutic shock and the vasculo-toxic effect of arsenicals.

### Prognosis

The prognosis is much more favourable when proper treatment has been carried out. With patients adequately treated after the detection of uncomplicated syphilitic aortitis, in a series of 267 cases (Padgett and Moore, 1936), 63 per cent were living and free from symptoms with no progression of cardio-vascular syphilis as compared with 49 per cent of those inadequately treated. Any form of specific anti-syphilitic therapy must be cautiously administered regardless of the degree of cardio-vascular involvement. Patients with frank symptoms must be treated with a greater degree of conservatism than those with more occult manifestations.

### Preventive treatment

The scope of this paper does not permit any discussion of the preventive treatment of syphilis, but the fact remains that it is one of those diseases where the golden maxim 'Prevention is better than cure' is vividly manifest. If proper precautions are taken, the disease can be wholly prevented: even when the disease has been contracted and detected early, its further progress could be arrested and the fatal lesions of syphilis in later life could be warded off.

### Treatment

Sequeira (1930) holds that there is hardly an absolute cure for untreated and inefficiently

treated syphilis, and the physician is, therefore, faced with the problem—once syphilitic always syphilitic.

The treatment should be done in two stages: In the first stage a pre-arsenical preparatory regime should be given which consists of the simultaneous administration of iodides or iodine and a heavy metal. If potassium iodide is chosen, it should begin with 5 gr. three times a day and gradually increased till 20 to 30 gr. are given per dose thrice daily. The course should be stopped after 6 weeks and then repeated. After an interval of 3 to 6 months, the serum and cerebro-spinal fluid should be tested, because a large number of cardio-aortic syphilis is associated with neuro-syphilis. As to the choice of the heavy metal, bismuth is the modern favourite on account of its superior anti-syphilitic power and its harmlessness. When there is a cardio-renal involvement, an insoluble bismuth salt in oil is the preparation generally used because of its slow absorption. The initial dose should not exceed 0.1 gm. given intramuscularly. Subsequent injections are given every 4 to 5 days in the beginning. Later the dosage is gradually increased to 0.2 gm. given once weekly. If mercury is given, it may be given in either of the two famous preparations, viz, the biniodide mixture or Hutchinson's pills.

The heart damaged by syphilis is in a bad metabolic condition. The administration of arsenicals decreases the rate of conduction and shortens the refractory period of the muscles; the latter acts indirectly by way of stimulation of the vagal nerve ending. Therefore, there is every danger of onset of ventricular tachycardia and ventricular fibrillation. Incomplete bundle branch block has been reported after the administration of arsenicals. Whether such a disaster is due to the rapid destruction of the luetic lesions and their replacement by scar tissue with injury to the intraventricular conducting system directly, to acute atresia, to closure of the mouths of the coronary arteries, or to ruptured aortic aneurysm is a matter of opinion. It is enough to know that such a sudden severe lethal therapeutic shock may happen.

The arsenical therapy should, therefore, only be given after a period of 3 months' preparatory treatment as mentioned above, and in every case the amount of cardiac reserve present must be revaluated. If it is found that the functional status of the circulation is inadequate, arsenicals are contra-indicated, for fear of Jarisch-Herxheimer reaction. When the cardiac reserve is moderate, it is better to begin with intramuscular injections of acetylarsan 1 e.cm. (containing 0.05 gm.) weekly and gradually increasing the dose to 0.15 gm. for 3 months. If adequate cardiac reserve is present, small doses of neo-arsphenamine may be given. The initial dose, interval and duration should be the same as that of acetylarsan, but it should be

given intravenously and no single dose of over 0.3 gm. should be given.

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## Medical News

## THE INDIAN HONOURS LIST

8TH JUNE, 1944

THE following are the names of medical men, and others associated with medical institutions, in the Indian Honours List of date 8th June, 1944. We offer them our congratulations.

## C.I.E.

Lieutenant-Colonel H. E. Murray, I.M.S., Professor of Midwifery, Medical College, and Superintendent, Medical College Hospitals, Calcutta.

## C.B.E.

J. B. Grant, Esq., Director, All-India Institute of Hygiene and Public Health, Calcutta.

## O.B.E.

J. Ray, Esq., Director of Drugs and Dressings, Medical Division, Department of Supply, Government of India.

## M.B.E.

Rai Bahadur S. K. Mukerji, Lecturer in Medicine, King Edward Medical School, Indore, Central India.

A. A. M. Wajih, Esq., Chief Medical Officer, Emergency Hospitals and Medical Supplies, Bengal.

*Kaisar-i-Hind Gold Medal*

Miss Evangeline Booth Crann, Sister-in-charge, A.R.P. Emergency Hospital, Behala, 24-Parganas District, Bengal.

*Bar to the Kaisar-i-Hind Gold Medal*

Miss Winifred Spicer, Matron, Bombay, Baroda and Central India Railway Hospital, Ajmer, and Lady Superintendent, Lady Minto's Indian Nursing Association, Rajputana Branch.

*Kaisar-i-Hind Silver Medal*

Miss Hannah Brooks, Nursing Superintendent, Mayo Hospital, Lahore, Punjab.

Miss Mary Agnes Burchard, Medical Missionary, Creighton-Freeman Christian Hospital, Brindaban, Muttra District, United Provinces.

Miss Wilhelmina Cracknell, Medical Missionary, Methodist Mission Hospital, Nadiad, Kaira District, Bombay.

Miss Frances Elizabeth Muriel Gregory, Lady Superintendent, St. George's Hospital Nursing Association, Bombay.

Miss Diana Hartley, General Secretary, Trained Nurses Association of India, New Delhi.

Miss Elizabeth Frances McConnell, Superintendent, Good Samaritan Hospital, Jhelum, Punjab.

Miss Muriel Stowe, Superintendent, Lady Lansdowne Hospital for Women, Bhopal, Central India.

Antonio Vincente Anacleto de Araujo, Esq., First Assistant Medical Officer, Mental Hospital, Nagpur, Central Provinces and Berar.

*Bar to the Kaisar-i-Hind Silver Medal*

Mrs. Dorothy Alayne Denholm Muirhead, W.V.S., Delhi, and Red Cross Representative, Delhi Cantonment.

*Kaisar-i-Hind Bronze Medal*

Mrs. Kamala Banerjee, Lady Doctor, Sadr Hospital, Chapra, Saran, Bihar.

Mrs. Berlie Diengdoh-Taylor, Vice-President, W.V.S., Shillong, Assam.

Mrs. Isa Boyd Gifford, Lady Divisional Superintendent, Delhi-Simla II Nursing Division of the St. John Ambulance Brigade Overseas No. X District.

Mrs. Edith Muriel Gill, Matron, Great Indian Peninsula Railway Hospital, Bombay.

Mrs. Elizabeth Lavender, Chairman, Poona and Kirkee Red Cross Depot, Bombay.

Miss Edith Frances Mason, Nursing Superintendent, Memorial Hospital, Ludhiana, Punjab.

Miss Muriel Raynor, Organizing Secretary, Madras Provincial Red Cross Branch, Madras.

Mrs. Norah Kathleen Warren, Honorary Secretary, Red Cross, Bareilly, United Provinces.

P. Adinarayanamurti, Esq., Medical Officer, Government Hospital, Kalahasti, Chittoor District, Madras.

N. K. Guha, Esq., Medical Practitioner, Narayanganj, Dacca District, Bengal.

M. K. Rahman, Esq., Sub-Assistant Surgeon, Gauhati, Assam.

*Diwan Bahadur*

Rao Bahadur K. K. Nayar, Superintendent, Government Ophthalmic Hospital, Medical Officer, Civil Orphan Asylum, and Professor of Ophthalmology, Medical College, Madras.

*Khan Bahadur*

M. A. Hamid, Esq., Professor of Pathology, King George's Medical College, and Provincial Pathologist, United Provinces.

*Rai Bahadur*

Rai Sahib B. P. Mital, Assistant Director of Public Health, United Provinces.

Rai Sahib L. N. Mathur, Honorary Dental Surgeon, K. E. Hospital, Benares, United Provinces.

Lala P. N. Dogra, Assistant Inspector-General of Civil Hospitals, Punjab.

B. K. Ray, Esq., Civil Surgeon, Bhagalpur, Bihar.

K. P. Sen Gupta, Esq., Lecturer (Retired), Robertson Medical School, Nagpur, Central Provinces and Berar.

M. C. Madhok, Esq., District Medical Officer, Bengal and Assam Railway, Kanchrapara.

*Rao Bahadur*

M. G. Kini, Esq., Professor of Surgery, Stanley Medical College, Superintendent and First Surgeon, Stanley Hospital, Medical Inspector of Emigrants and Surgeon, First District, Madras.

Rao Sahib A. S. Barot, Medical Practitioner, Dohad, Broach and Panch Mahals District, Bombay.

*Khan Sahib*

Maulvi Samsuzzaman, Medical Practitioner and Honorary Magistrate, Amta, Howrah, Bengal.

M. H. Khan, Esq., Private Medical Practitioner, Moradabad, United Provinces.

J. D. Muhammad, I.M.D. (Retired), First Grade Sub-Assistant Surgeon, Civil Medical Department, Baluchistan.

*Rai Sahib*

S. C. Dutta, Esq., Sub-Assistant Surgeon, Krishnagar Sadar Hospital, Nadia, Bengal.

R. G. Rudra, Esq., Medical Practitioner, Ghatal, Midnapore, Bengal.

A. S. Dikshit, Esq., Medical Officer, Cholera Vaccine Section, Hygiene Institute, United Provinces.

Lala S. C. Vinyek, Medical Practitioner, Honorary Secretary, Ferozepore Central Co-operative Bank, Limited, Ferozepore, Punjab.

G. S. Pathak, Esq., Sub-Assistant Surgeon and Recruiting Medical Officer, I. A. M. C., Bihar.

Dr. B. Narayan, Professor of Physiology, Prince of Wales Medical College, Patna, Bihar.

*Rao Sahib*

K. S. R. Ranganathan, Esq., Provincial Blood Transfusion Officer, King Institute, Guindy, Chingleput District, Madras.

D. M. Sivasubrahmanyam, Esq., Additional Professor of Anatomy, Central Institute of Anatomy, Physiology, Organic Chemistry and Biochemistry, Medical College, Madras.

U. B. Narmannao, Esq., Medical Practitioner, Bombay.

D. Manuel, Esq., Sub-Assistant Surgeon, Civil Medical Department, Burma.

J. V. Takle, Esq., Extra Assistant Director In-charge, Animal Husbandry Section, Veterinary Department, Central Provinces and Berar.

*O.B.I.*

*To the First Class with the Title of 'Sardar Bahadur'*  
Indian Army Medical Corps

Subedar-Major Sudhireswar Sen Gupta, Bahadur, O.B.I.

Subedar-Major Guran Ditta Bahadur, O.B.I.

Subedar-Major and Honorary Lieutenant Shankar Krishna Gole, Bahadur, O.B.I.

Subedar-Major Vasant Sakharan Gaikawad, Bahadur, O.B.I.

Subedar-Major and Honorary Lieutenant Bhupendra Nath Lahiri, Bahadur, O.B.I.

Subedar-Major Jawand Singh, Bahadur, O.B.I.

Subedar Rao Sahib Chingleput Manikham, Bahadur, O.B.I.

Subedar Karim Bakhsh, Bahadur, O.B.I.

Subedar Yaqub Ali, Bahadur, O.B.I.

Subedar-Major Kuppaswami Panchanadham Pillai, Bahadur, O.B.I.

Subedar-Major Puran Singh, Bahadur, O.B.I.

*To the Second Class with the Title of 'Bahadur'*  
Indian Army Medical Corps

Subedar Partap Singh.

Subedar-Major Ponnuswami Dinadayalan.

Subedar-Major Babu Singh.

Subedar-Major Muhammad Tasawar Khan Afridi.

Subedar-Major Amar Nath Chopra.

Subedar Pritam Singh.

Subedar-Major Mathura Pershad Soti.

Subedar-Major Arjun Singh Dhillon.

Subedar-Major Arjan Singh Sekhon.

Subedar-Major Inder Singh.

Subedar-Major Shambhu Chidamber Padki.

Subedar-Major Sri Krishna Vashistha.

Subedar Balwant Singh.

Subedar Bishan Das Minocha.

Subedar-Major Vinayak Narayan Denskar.

Subedar-Major Narsingh Das Khurana.

Subedar Hazura Singh Grewal.

Subedar Kartar Singh Grewal.

Subedar Nand Kumar Tiwari.

Subedar Muhammad Afzal Khan.

Subedar-Major Hirde Narain.

Subedar-Major Faqir Chand Kapila.

Subedar Vishan Dass Sharma, M.B.E.

Subedar Rama Nand.

Subedar Mahtab Singh, M.B.E.

# INDIAN CHEMICAL MANUFACTURERS' ASSOCIATION: REPORT OF THE COMMITTEE FOR THE YEAR 1941-42

'THE war has undoubtedly given impetus for the development of the chemical and pharmaceutical industry', said Mr. J. N. Lahiri, President of the Association, at its fourth annual general meeting held at Delhi in November 1942, but the main difficulty is that it has to depend for almost all important items on import from foreign countries, although India abounds in all kinds of raw materials of mineral, animal and vegetable origin. He spoke of the slow development of mineral and chemical industries in the face of many difficulties, and quoted, as an example of neglect and indifference, the case of glucose, tons of which are imported from America, and hardly any attempt is made to manufacture it in India in spite of the abundance of cereals.

The pharmaceutical industry is in a much better position than during the last war, and India is now producing all ordinary chemicals and essential B.P. drugs, vaccines and sera, but it has yet to make headway in chemotherapeutic products, vitamins and hormones. The chief difficulty with regard to the latter is that, as these drugs are primarily chemicals, their manufacture will be conditioned by the development of the chemical industry in general; besides sufficient raw materials and intermediates must be obtained before complicated chemicals can be synthesized. Mr. Lahiri gave the example of atebrian (mepacrine B.P.) in the manufacture of which 23 chemical compounds are involved, and in the making of 1 pound of atebrian approximately 46 pounds of raw materials are required. Yet this difficult synthetic compound has already been prepared in India, but it cannot be made in sufficient quantities until the dependency on imported intermediates is removed. A few substitutes, e.g. neosalvarsan, carbarsone, luminal, atophan, sulphanylamide, etc., have also been made showing that Indian chemists are competent to undertake their manufacture successfully.

Talking of quinine supply, the Government, he said, should not hesitate in increasing cinchona plantations in suitable areas. The total area under cinchona in Bengal during 1939-40 was only 3,168 acres, and during 1937-38, 51,839 pounds were locally manufactured; Bengal alone can absorb 350,000 pounds a year. If it is true that the cinchona plantations in Java which used to supply 93 per cent of quinine supply of the world have been efficiently scorched, then the quinine famine is bound to last for many more years to come, as under ordinary conditions, cinchona bark suitable for extraction of alkaloids is obtainable only from trees 10 years old. From scientific reports, it seems perfectly feasible to take measures for increasing the alkaloidal content of Indian cinchona. This has been achieved in Java by giving a suitable species of *C. ledgeriana*, and Russia has succeeded, by suitable grafting and transplantation, in getting a fair yield of quinine within a comparatively short period.

## Public Health Section

## EPIDEMIOLOGY OF CHOLERA IN THE PUNJAB\*

By KHAN BAHADUR M. YACOB, M.B., B.S. (Pb.),  
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CHOLERA belongs to the group of infectious diseases known as the 'big five', namely, malaria, influenza, plague, smallpox and cholera, which display the phenomenon of epidemicity to a conspicuous degree. In many parts of the world, and most of all in this country, where the disease is liable to assume epidemic proportions from time to time and destroy thousands of people, the word 'cholera', on account of the sudden onset of the disease, its rapid course and in many cases an equally sudden and dramatic fatality, is associated with a feeling of dread in the human mind.

In order to understand the epidemiology of cholera in the Punjab, and to appreciate correctly the part that this province has so far played and is likely to play in the coming years in the prevention of the disease, it is necessary, in the first place, to have a clear picture of the general incidence of the disease in India as well as in the adjoining countries. We need not go very far away from India, because in more recent times almost all the western countries, as also some of the advanced countries of the east, have succeeded in getting completely rid of this disease which at one time was responsible for an alarmingly high incidence all over the world. To some extent, even at present, a study of the geographical distribution of cholera in the world is hindered by lack of reliable data, and this is particularly so in Asia where alone the disease still remains entrenched in a position of vantage. Nevertheless, a fairly satisfactory idea of the distribution of cholera in the world

is given in map 1 which has been prepared with some modification from a map which appeared in 1939 in the *Weekly Epidemiological Records* of the League of Nations (No. R. H. 705). All those areas which reported cholera during the period from 1930 to 1938 have been coloured black. Affected areas include practically the whole of India, the major portion of Afghanistan and certain portions of Iran, Iraq, Burma, Siam, Malaya, Indo-China, China, Korea, Japan and the Philippines. A noteworthy feature is the general absence of the disease from the Netherlands Indies. The strict anti-cholera measures adopted by the health authorities of these islands, and the insular position that these areas enjoy, are responsible for the absence of the disease. The difference between British India and the Netherlands Indies is indeed striking. Whilst our country is the hot bed of the disease, our neighbours enjoy complete freedom. It may not be out of place to reproduce here what the Public Health Commissioner with the Government of India quoted in his report for the year 1938 (Cotter, 1941) from a pamphlet entitled 'The eradication of cholera and the campaign against

MAP 1

Showing geographical distribution of cholera from 1930 onwards



smallpox in Netherlands Indies'. This is an extract.

'The population of British India in 1921 was 318,942,000 and of Java and Madoera 34,984,171 in 1920. We find from the table by summation that during the years 1923 to 1934, the number of deaths from cholera in British India was 2,490,409 and for Java and Madoera only 17, of which 16 were in the year 1927 and one in

\* Being a paper read at the Annual General Meeting of the British Medical Association, Punjab Branch, Lahore, on the 16th March, 1944.

1928. It seems evident that the great improvement in the Netherlands Indies, as regards cholera, must be set down to the introduction of pipe water supplies, reorganization of the public health service, large-scale vaccination, insistence on certificates of vaccination for immigrants, and strict quarantine regulations.'

The Public Health Commissioner with the Government of India further stated that 'India has to make considerable progress before attaining such conspicuous success in the campaign against cholera'.

We must take note of the fact that now the one important home of cholera in the world is India. Historical records further bear out that the disease has existed in this country since the remote past.

Macnamara (1870) believes that the disease described as 'vishuka' by Susruta in the sixth century B.C. was identical with Asiatic cholera. The characteristics attributed by Susruta to the disease are severe purging, vomiting and consequent exhaustion, suppression of the voice, sunken eyes, coldness of the body and a high fatality. The first European to give a description of cholera was a Portuguese named Correa, who stated that during the year 1503, about 20,000 men died of cholera in the Army of the Sovereign of Calicut. The same author describes a similar epidemic at Goa in 1543. In 1563, d'Orta, another Portuguese, described an epidemic in Goa of a disease known as 'Haiza' to the Arabs. As a matter of fact, 'Haiza' is the vernacular equivalent of cholera and the term is in use even at the present day in India. In 1589, an outbreak of a highly fatal disease characterized by severe vomiting and purging was described by Linchot, a Dutchman, as having occurred at Goa. The first Englishman to describe cholera in India was Paisley who wrote of an epidemic in 1774. In 1781, Pearson, an English army officer, whilst marching with troops through the district of Ganjam, described his experience as follows:—

'Death raged in the camp with horror not to be described, and all expected to be devoured by the pestilence. In vain I studied to discover the cause of our misfortune. I attributed it to a poison, but at length found that there had been a pestilential disorder raging in the parts through which our first marches lay, and that part of our camp was always drinking the air of death and destruction.'

Macnamara further refers to an epidemic which broke out in Hardwar in 1783 amongst the pilgrims and caused 20,000 deaths within a period of a week. This author, after studying the history of cholera in India prior to 1816, concludes as follows:—

'We are, therefore, I think justified in arriving at the conclusion that it was nothing new for cholera to spread over India in an epidemic form prior to 1817 and 1819. The nature of the disease was then for the first time recognized, and as the greater portion of the country had passed under our rule, British officers were in a position to trace the progress of the disease over the length and breadth of the land.'

Coming to more recent times, we know that an epidemic of cholera originated in Bengal in 1817, spread towards the north in the United Provinces and the Punjab in 1818 and also occurred in epidemic form in the Central Provinces, Bombay Presidency and afterwards in the whole of the peninsula culminating in the worst epidemic known (Rogers and Megaw, 1942). The first pandemic which swept the entire world also originated in Bengal, spread through the Punjab in 1826 into Central Asia by the overland route through Afghanistan and Persia, reached Europe in 1830 through South Russia and travelled as far as America in 1832.

Another pandemic which spread by the same route through the Punjab and then into Europe in 1840 to 1849 is stated to have killed as many as a million persons in Europe alone and was responsible for 53,293 deaths in England. Another spread through the Punjab and then into Europe occurred in 1866 to 1870. The latest epidemic to have travelled up from Bengal through the Punjab into Afghanistan occurred in the year 1941. There is no doubt, therefore, that the Punjab has been one of the important gateways through which infection escaped to cause ravages in almost the whole world in the past.

The years intervening between any two virulent and widespread epidemics of the disease were by no means years of freedom either for the whole of India or even for the Punjab. Since the year 1867 the Punjab has been preserving a continuous series of statistical records relating to the mortality caused by this disease in this province, and the other provincial governments have been doing the same in respect of their areas. From a study of these it becomes clear that so far, during these last 77 years, not a single year has passed in which cholera has not caused some mortality in some part of India. Even the Punjab has so far not recorded any year in which deaths from cholera did not occur. And this state of affairs has continued to exist in spite of the existence for some decades now of fairly well developed public health organizations in all the provinces and in all the larger Indian States as well as the continued existence of a central co-ordinating and directing authority in the Public Health Commissioner with the Government of India.

None of the outbreaks in India can be regarded as having originated from infection imported from outside India. There should, therefore, be no doubt that India was and still continues to be an important, if not the only, endemic home for cholera in the world. That being so, we must ask ourselves whether the distribution of the disease throughout the length and breadth of this vast subcontinent is similar, or whether the disease has a tendency to persist only in certain specific localized regions.

Among the earlier workers who studied this question of endemicity mention must be made of the names of Bryden, Macnamara and Bellew. Bryden who was the statistical officer with the Sanitary Commissioner published a voluminous report on cholera. His endemic area comprised the western part of Assam, all the regions of lower Bengal and Orissa up to the low Rajmahal and Cuttack hills to the west of this basin as well as eastern Bihar. Bellew's study (1885) of this problem of endemicity was equally laborious. He studied the statistical records from 1862 to 1881 available from the official reports. His main thesis is:—

'Cholera in India is a disease which, in point of prevalence, is very intimately related to, and dependent upon, the climatic and seasonal influences of the country, and that the effects of these influences, as manifested in the prevalence and fatality of the disease, are in a very remarkable manner modified and controlled by conditions of locality affecting the soil, the



weather, and the life-circumstances of the people.' Thus he also clearly recognized that only specific localities were capable of harbouring the infection for continued periods. In the endemic areas of cholera he states :—

'The main features of the physical geography are characterized by a low-lying alluvial soil, which is more or less supersaturated with ground water in a state of stagnation or but comparatively very slight motion, and which is subject to periodical inundations or water-logging by the seasonal floodings of the great rivers by which those areas are traversed in deltaic formation. These physical characteristics of the endemic areas are coupled with equally striking features characteristic of their climatic conditions, viz, with those of a moist and hot tropical or sub-tropical climate, and they are among the most densely populated parts of the country. Examples of such areas in Bengal and Assam are the great river deltas of the Ganges and the Brahmaputra, of the Mahanadi in Orissa and the interfluvial tracts of Bihar and in Madras by those of the Godavari, the Kistna and the Cauvery. In the southern portion of the Bombay sea board, however, as on the Konkan and Malabar coasts, the littoral assimilates in physical characteristics both of soil and climate to the great deltaic areas of Bengal and Madras and we find that these tracts also are more or less strictly endemic areas of cholera. In the North-Western Provinces and Oudh we find in the area of the convergence towards the Ganges of the several great rivers by which those provinces are watered a state of country which bears many points of resemblance to the deltaic regions of Bengal; in conjunction, too, with a climate partaking of both tropical and extra-tropical characteristics—the climate of the southern half of the region assimilating to that of Bengal, and of the northern half to that of the Punjab. In the former extensive tract of country, which includes Oudh and the southern Gangetic districts of the North-Western Provinces as far up as Allahabad, the characteristic features of the physical geography are an alluvial plain and a soil more or less highly saturated with ground water, the subsoil level of which is comparatively close to the surface, as is evidenced by the general use of lever wells for purposes of field irrigation. Its climate, also, bears some resemblance to that of the adjoining portion of Bengal, more especially during the season of the hot weather monsoon rains. Its population, too, is quite as densely massed, if it is adjoining to it. In the southern half of this province cholera is considered to be an endemic disease because of its persistent presence at all times and seasons. In the latter, or northern half of these territories, whilst the physical aspect of the plain country differs little from that of the corresponding part of the southern half, the climate presents some marked differences, with a generally less humid atmosphere and a decidedly colder winter season, whilst its population is decidedly less densely massed, and enjoys also a better condition of material prosperity than that in the southern half. In this portion, also, cholera is found to be an endemic disease, although to a less extent than in the southern half.'

'In the Punjab, we find no great alluvial tracts corresponding to those of the Gangetic, river basin, nor similarly affected by fluvial agencies. The hydrographic system of the Punjab centres in the Indus, and the confluence of its great tributaries and their lesser affluents is effected without the production of any great areas of low-lying waterlogged alluvium in conjunction with a comparatively humid and hot climate, as is the case in the North-Western Provinces and Oudh, since the rivers, in their course obliquely across its great plain, are separated by great dorsal ridges of more or less entirely arid tablelands which very clearly define the lowland strips of the several river valleys. These lowland strips are subject more or less to inundation from their respective rivers in the flood season, and are generally at all times more or less saturated with ground water by percolation from their streams. But the climate, being clearly extra-tropical, is so unusually dry, owing to the vast area

covered by thirsty deserts and arid tablelands within the limits of the province and beyond its southern borders, that the natural humidity of these lowland strips is quite lost in the general aridity around. Nevertheless there are some tracts in the Punjab which bear a close resemblance to some parts of Bengal and the North-Western Provinces in respect to the relatively low level of the land and the supersaturation of its surface soil with ground water, as well as in respect to climate during the season of the hot weather monsoon rains, but during this season only. Such tracts are found in the Gurgaon, Delhi, and Karnal districts between the diverging Jumna and Sutlej rivers; in the Kangra, Gurdaspur, and Amritsar districts between the converging Beas and Ravi rivers; also in the Hoshiarpur and Jullundur districts of the Beas and Sutlej interfluvial tract. All these tracts in the Punjab are favourite haunts of cholera both in epidemic and ordinary seasons, and the disease is sometimes so mixed up with the endemic malarious fevers of the tracts as to be indistinguishable from the more prevalent fevers.'

Sufficient and reliable statistical data did not exist at the time when Bryden and Bellew made their studies. In more recent years, Rogers has tried to study more complete statistical data for 45 years for each of the 45 separate divisions into which the whole of India was divided by him. His researches have been published in Memoir No. 9 of the *Indian Journal of Medical Research* (1928). The endemic areas defined by him include the following :—

- (i) a very large north-east area comprising all Assam, Bengal and Bihar and the eastern divisions of the United Provinces; this area being twice as large as the one defined by Bryden;
- (ii) a large area comprising the central and south-east coast districts of the Madras Presidency; and
- (iii) the narrow hot and damp Konkan coast of Bombay.

Another fairly extensive and recent study involving the application of modern statistical methods was carried out by Russell and Sunderarajan (1928). Their researches have also been published in Memoir No. 12 of the *Indian Journal of Medical Research*. The endemic areas defined by them also include Assam, Bengal and certain areas of Madras Presidency. They further state that certain provinces may be said to be neither endemic nor epidemic, for the reason that they only occasionally suffer from cholera when infection is carried in from outside chiefly in the rainy season. The Punjab, according to them, belongs to this group. We may also refer here to the view expressed by Gill (1926); one of the pioneers of epidemiology in the Punjab. He believed that no permanent foci of cholera are known to exist in the Punjab, and in almost every instance, outbreaks of cholera in this province were directly or indirectly traceable to importation of infection from outside.

Even up to the present day, India continues to harbour the endemic zones of cholera, but the Punjab is not one of those zones, although this province lies on the route of spread of cholera from India to other countries on the west. This point will be better appreciated when it is made clear that ever since historical



records of cholera have been kept, the direction and the route of spread of the disease have remained unchanged. Russell and Sunderarajan (1928) states: 'It seems certain that a wave can start from Bengal and proceed west and south-west, but it is not possible for a similar wave

shape of the seasonal mortality curves is concerned, therefore, the map shows comparable charts. On the assumption that 1,000 deaths from cholera occurred in a year, the distribution of the deaths in each province would be as shown in the following table:—

Table showing the distribution of 1,000 annual cholera deaths by months in each province

Provinces	January	February	March	April	May	June	July	August	September	October	November	December
N. W. F. Province ..	32	..	..	1	114	224	141	189	222	45	15	17
Delhi ..	..	2	4	36	186	133	353	68	24	160	28	6
United Provinces ..	4	3	10	45	148	228	169	143	94	78	54	24
Bengal ..	83	64	148	177	86	39	32	31	42	58	107	133
Bihar ..	10	16	21	45	56	79	113	145	112	135	190	79
Orissa ..	59	54	66	58	71	65	74	75	102	109	124	143
Central Provinces ..	2	4	10	78	92	88	161	245	209	84	20	7
Bombay ..	18	11	8	20	52	51	121	245	211	120	92	51
Madras ..	101	107	60	58	36	41	65	93	84	69	93	103
Assam ..	99	40	40	108	148	103	56	42	53	69	112	130
Sind ..	..	..	..	3	199	358	331	101	8	..	..	..
Punjab ..	..	..	..	42	294	299	159	139	50	14	3	..

to start in the southern district of Madras and proceed north or north-west'. They further quote the Sanitary Commissioner for the Punjab who has stated that 'there has never been recorded an epidemic travelling to Lahore from Multan on the south-west or from Peshawar on the north-west'.

Bryden also recorded repeated instances when cholera spread across India, from what he termed its endemic home in lower Bengal, by two main routes called by him the 'northern epidemic highway' up the Ganges valley to Afghanistan and Persia, and the 'southern epidemic highway' across the Central Provinces to the south. Punjab is one of the provinces to fall on Bryden's 'northern epidemic highway'. Fry (1925) has remarked that in no single year during the period 1817 to 1872, did cholera spread in the reverse direction. Thus the danger to the Punjab has invariably been from the south-east. This danger is further aggravated by one single and extremely important factor, viz, the pilgrimage to Hardwar. This factor is discussed subsequently. In connection with the direction and the route of spread, however, the seasonal variation of cholera mortality in the different provinces is of special interest.

In map 2 the seasonal mortality curve of each province in India has been charted. For the estimation of these seasonal curves, the monthly cholera mortality records for the five-year period, 1935 to 1939, the latest available, have been taken and the total monthly deaths over these five years calculated. These are based on different populations. For the sake of comparison, each of these averages of the 12 months has been increased or decreased proportionately so as to yield for each province a total number of 1,000 deaths. In so far as the

In Bengal if 1,000 deaths were to occur in a year, the maximum number of 177 should be expected to occur in April. Deaths continue to occur throughout the year and the minimum average figure is 31 in the month of August. The seasonal curve is, therefore, characterized by low peaks and a more even distribution. The season of high cholera is from November to May and in fact a rise in cholera mortality sets in sometimes in September. Coming westwards to Bihar, the period of high incidence begins earlier in July and the peak is reached in August during the monsoon season. This peak has hardly time to subside when another rise sets in and extends throughout the winter. In the United Provinces the same trend in the change of seasonal curve is seen to be in operation. The season starts still earlier, i.e. from May onwards, and although the winter incidence is lower than in Bihar and very much lower than in Bengal, the mortality from cholera is not wholly absent. In the United Provinces a curve that rises in May dies out only slowly. Coming to the Punjab the winter portion of the curve is further suppressed and the incidence reaches its maximum in May and June. The same remarks apply to Sind and the N. W. F. Province. Generally speaking, therefore, we may conclude that from Assam and Bengal cholera proceeds to Bihar and Orissa in March and April, to the United Provinces in April and May and to the Punjab and the N. W. F. Province in May, June, July and August.

The geographical distribution of cholera throughout India represents in a general way the considerably decreased incidence of the disease as we pass from the eastern to the western provinces. This is what should be expected particularly in more recent years when the better organized public health departments

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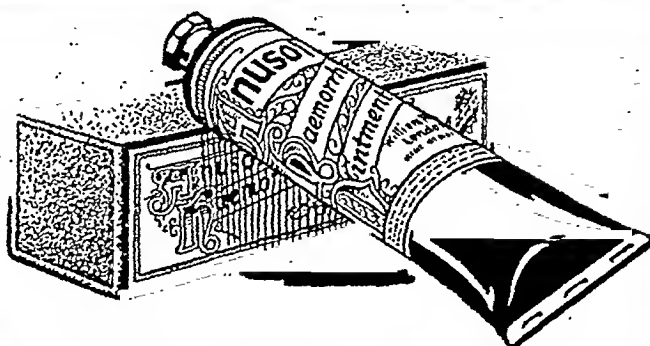
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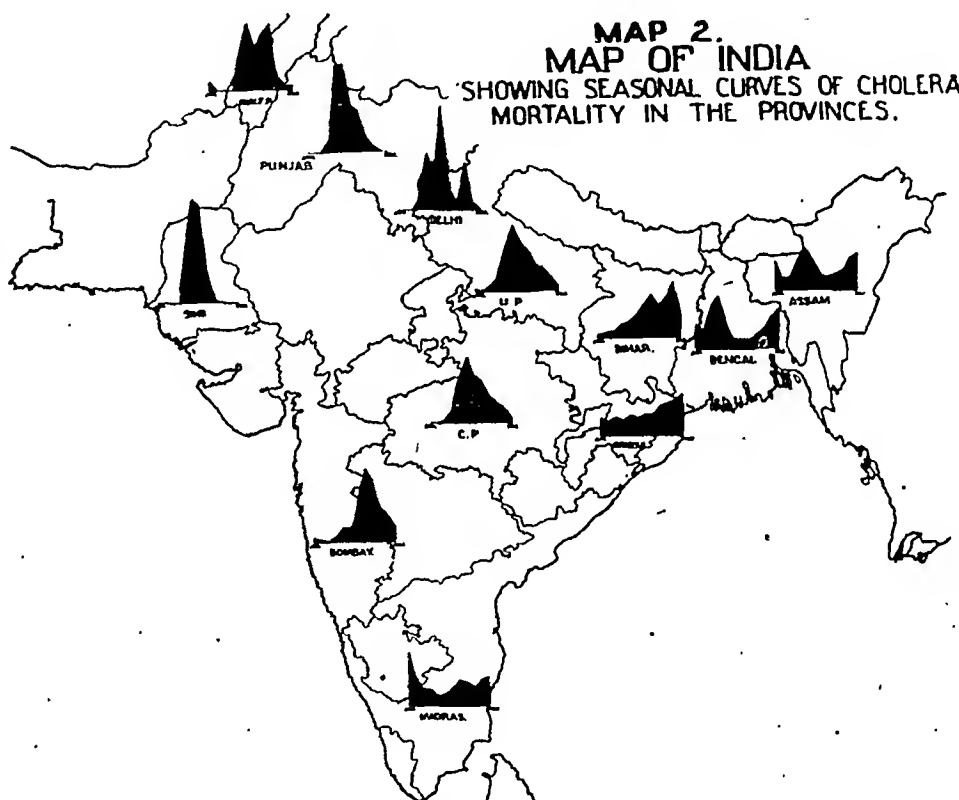
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devote considerable attention to fighting this disease. Had it not been for the presence of some of the important pilgrimage centres and especially Hardwar and Benares and Allahabad in the United Provinces the gradual reduction in the mortality from the east to west in India would have been even more clearly marked. Every year thousands of devotees assemble at these places, and infection from different areas is thus carried to one central place only to be disseminated, sometimes most widely, in all directions of communications. To the Punjab, the danger from such dissemination is considerable. The Public Health Department is fully aware of this danger, and every attempt is made to check the importation and spread of the disease in the province. Usually infection is brought from Hardwar, and even up to the last year it was not uncommon to hear of cases of cholera being removed from the trains. Occasionally even dead bodies of persons who had boarded trains hale and hearty but could not survive a night's journey up to Lahore have had to be removed at the intervening railway stations. The eastern districts of the Punjab, which lie on the route of the pilgrimage to Hardwar, show, as should be expected, a relatively higher incidence of cholera. The highest incidence is recorded by Lahore district because Lahore, on account of its being the central railway junction, forms the most important link between Hardwar and the rest of the province; and almost all the pilgrims to western and south-western districts must pass through this place thus spreading infection into the towns and rural parts of the Lahore districts. The eastern half of the Punjab is shown to have generally a higher incidence than the western Punjab, the reason being that the majority of the pilgrims belong to the eastern Hindu districts.

In chart 1, which shows the annual cholera mortality figures from 1867 onwards, the whole recorded history of cholera in the Punjab has been traced. The height of each bar erected against each year denotes the cholera mortality rate per 1,000 of the estimated population of that year. The bars are shown in different shades to indicate briefly the major causes of the outbreak of epidemic each year. It must be mentioned that every six years a vast con-

gregation of pilgrims is held at Hardwar at the time of the *Kumbh* fair. This mass gathering is not without its effect on the cholera history of the Punjab. The outbreaks which followed the *Kumbh* fairs have been shown by thick black bars. With a few notable exceptions, the chief of which is the year 1892, the majority of the epidemic years were those in which the *Kumbh* fairs were held at Hardwar, and specially is this the case in recent years which have otherwise been, relatively speaking, fairly free from the disease. Of all the black bars, the highest relates to the earliest year 1867. Since then, a gradual tendency towards decrease is noticeable in the height of these bars which indicates that with the progress of time each *Kumbh* fair has been better controlled. The last fair was held in 1938; and the bar is fairly



low in comparison with the previous *Kumbh* years.

It is not perhaps generally known that the danger from Hardwar does not arise only after every six years, but is perennial. The annual *Baisakhi* fair which is held in each April and, unfortunately, shortly before the onset of the cholera season in the Punjab also attracts a fairly large number of pilgrims from this province who in the non-*Kumbh* years are instrumental in the spread of cholera in the province. The bars with slant hatching signify that in non-*Kumbh* years Hardwar again was responsible for the spread of the disease. The highest bar is for the year 1892 which followed a *Kumbh* year. Infection which had taken root in Hardwar in the *Kumbh* year of 1891 persisted throughout that year and reached Punjab

only during the following year. The pilgrims from the Punjab during the next year, therefore, brought in the infection which had failed to spread in 1891.

Cholera is a disease largely associated with mass gatherings, and it is therefore to be expected that fairs within the province, such as

reported as cholera may have been due to food poisoning or to other gastro-intestinal disturbances and even in certain instances to arsenical or mercurial poisons administered with criminal intent.

The salient feature of this chart is that, as a rule, cholera in the Punjab is of an imported

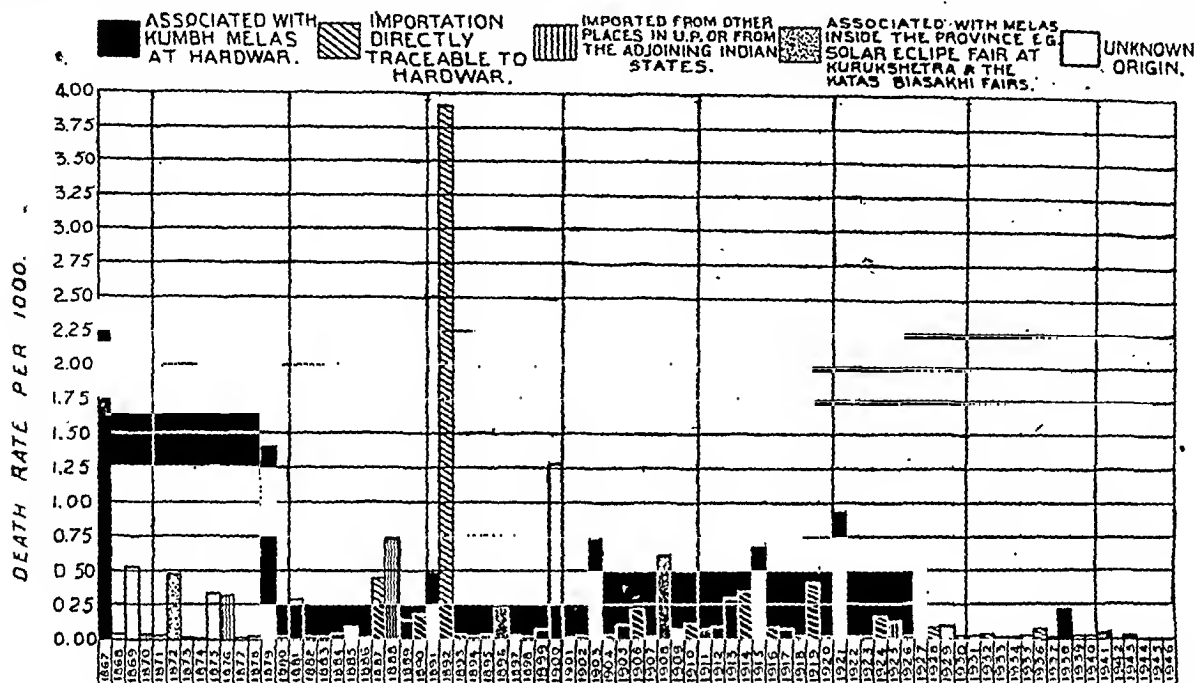


Chart 1 showing cholera mortality in the Punjab from 1867 onwards.

those associated with the solar eclipse at Kurukshetra and the *Katas Baisakhi* fair, should also play their part in the spread of the disease. The bars for those years in which fairs within the province were responsible for the spread are shown dotted. The number of such cases is not large, and is insignificant in recent years. It is significant to remark in this connection that the most recent solar eclipse fair at Thanesar held in 1941 passed off without a single case of cholera. The fair was attended by approximately 500,000 pilgrims.

The bars with vertical hatching relate to years in which infection was imported into the Punjab from places other than Hardwar. Some of these places are the adjoining southern Indian States, the other pilgrimage centres in the United Provinces and in the north the State of Kashmir.

All those years in which the outbreaks were of doubtful origin have been shown by blank bars. These, therefore, represent years in which importation may have occurred but could not be established as well as those years in which the disease might be regarded as of indigenous origin. The heights attained by these bars are generally low, the only exception being the year 1900. It must also be remembered that a correct diagnosis of true cholera is difficult at the hands of the generally illiterate reporting agency in the Punjab, namely, the village chaukidar, and it is not unlikely that many of the cases

nature and that Hardwar constitutes the biggest threat to its spread in this province.

The position that the province now occupies in respect of cholera mortality when compared with other provinces will become clear by a reference to the bar diagram shown in chart 2 in which the mean experience of the quinquennium 1936 to 1940 has been charted. Provinces which have higher rates of cholera mortality than the average rate for British India are Bengal, Orissa, the Central Provinces, Assam and the United Provinces, Bihar, Madras and Bombay also rank fairly high, whilst the Punjab is much lower down in the scale.

It would seem to be appropriate to refer here briefly to another aspect of the cholera question; namely, the serological diagnosis of *Vibrio cholerae*. This point is of basic importance as unless it is settled beyond doubt and certain means are found for the recognition of the choleric vibrio, no progress worth the name can be expected in investigations on the epidemiology of cholera involving the study of the relationship of the vibrio to the cholera case and the epidemic, and of the conditions under which *V. cholerae* exists and is transmitted as an infective agent. The work of Gardner and Venkataraman (1935) in England and that of Taylor and his co-workers in India during the years 1934 to 1940, under the auspices of the Indian Research Fund Association, has definitely established that cholera, whether in

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sporadic or epidemic form, is caused by vibrios which possess a characteristic heat-stable antigen. The majority of these vibrios belong to group I with Inaba and Ogawa sub-types.

An investigation undertaken in the laboratory of the Punjab Epidemiological Bureau during 1940 and 1941, when 65 strains of vibrios isolated during the course of outbreaks of cholera from various parts of the province showed that 55 of these were agglutinable with Inaba serum, whilst the rest were inagglutinable. All the agglutinable strains were found to belong to Heiberg type 1, *viz*, mannose +, arabinose -, saccharose +. Thus, all the available evidence points to the conclusion that only one type of vibrio is the cause of cholera and this conclusion has been accepted by the Office International d'Hygiene Publique as the basis for the application of quarantine measures (Taylor, 1941).

We must now come to the crux of the problem, which is the control of cholera and its spread from endemic areas in certain provinces to that of the Punjab, a non-endemic area. From what has been said above, it is clear that epidemics of cholera continue to occur after the *Kumbh* fairs in spite of care, lavish and expenditure on ordinary routine measures in regard to the festival area itself. Attention to this aspect of the question was first drawn by Rogers (Rajan *et al.*, 1940) when he claimed that the outbreak of an epidemic, in spite of these measures, proved his contention that nothing less than protection by inoculation of the pilgrims going to and from the fairs can possibly stop the regularly occurring epidemics from Hardwar and similar other pilgrimage centres in India. He emphasized, and rightly so, that the sanitation at a fair itself, even though properly looked after, is an altogether minor factor in the spread and diffusion of an epidemic, compared with the passage of millions of pilgrims travelling to and from through insanitary areas in which cholera is endemic. Rogers further emphasized that sanitation work in India during the previous 50 years had failed to reduce materially the incidence of cholera as a whole, for the obvious reason that it was practically impossible to provide protected water supplies and conservancy in the innumerable villages through which pilgrims have to pass. The remedy suggested by him for this unsatisfactory state of affairs was the utilization of mass inoculation. Recently, this thesis has found added support in the recommendations of the Report of the Sub-Committee (Rajan *et al.*, 1940), appointed by the Central Advisory Board of Health to examine the possibility of introducing a system of compulsory inoculation of pilgrims against cholera. The committee has recommended that

the provincial health authorities should give adequate notice to the inhabitants of areas from which pilgrims are likely to proceed to various pilgrim centres that they will be prohibited from entering the fair area unless they can produce proof of inoculation. At the same time, the necessary facilities should be provided in these areas to enable the pilgrims to get inoculated conveniently. Further, the provincial government should prevent the departure from their province of any pilgrim who has not been inoculated.

The above recommendations of the Central Advisory Board of Health constitute an administrative measure of an outstanding importance in the prevention, control and dissemination of cholera from one province to another. Arguments against the advisability of the introduction of compulsory inoculation against cholera are bound to be put forward by the opponents of this method of prophylaxis based on unwillingness or resistance against such a

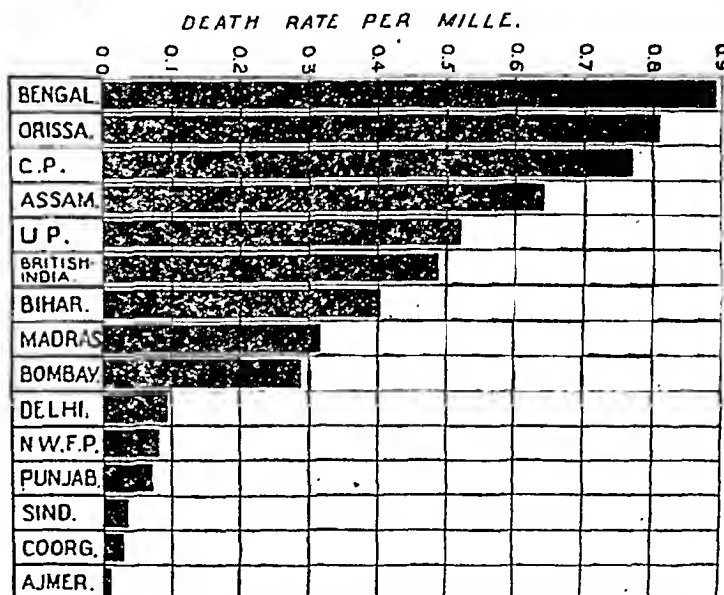


Chart 2 showing cholera mortality rate in the provinces and in British India during 1936-1940.

measure on the part of pilgrims, the prohibitive-ness of the cost of carrying it out and on the difficulties of organization. These, however, must be brushed aside, and it should not be beyond the ingenuity and resources of the provincial government, the public health authorities in this province and the railway administration to devise ways and means to achieve the object in view. As a matter of fact, the stakes at issue are so important in terms of human lives that 'nothing short of impossibility should be allowed to come in the way of an adequate solution of the problem'. For this purpose a radical change in our sanitary outlook is essential. There is no reason why we should complacently and pathetically accept the view that cholera has been in this country from time immemorial and will always continue to remain with us.

**Acknowledgments**

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**Current Topics****Alkalis in Sulphonamide Therapy**

(From the *Lancet*, i, 4th March, 1944, p. 318)

THE antibacterial activity of sulphonamides has been shown to depend on their degree of ionization. Therapeutic activity is exerted by the sulphonamide anion while the undissociated molecule is relatively inactive. It has also been shown that raising the pH of sulphonamide solutions to neutral or alkaline levels by increasing their degree of ionization will increase their activity in proportion. Furthermore the greater potency of sulphadiazine and sulphathiazole as compared to sulphapyridine and sulphanilamide is explicable by their greater degree of ionization at pH 7.4. These observations have now been applied to the local use of sulphonamides in wounds and burns and the influence of alkalis on the solubility of these drugs has been studied with a view to preventing precipitation in the urinary tract. The solubility of sulphapyridine and sulphaguanidine is not much altered by making the urine alkaline within the physiological range, but Jensen and Fox have found that sulphathiazole and sulphadiazine, like other weak acids, are made much more soluble by the addition of alkali. Their solubility in urine is minimal from pH 5.6 to 6.6, doubled or tripled at pH 7.5 and increased tenfold at pH 8.0. In a patient receiving a sulphonamide the glomerular filtrate contains a concentration of sulphonamide approximating to that in the blood and sharing a similar pH (7.4). As this filtrate progresses through the tubular part of the nephron, many constituents, especially water, are reabsorbed. This process leads to a rapid rise in the concentration of the sulphonamide in the urine and to a concurrent fall in pH to the normal acid levels (between 5.0 and 6.0) of voided urine. As a result, crystals may be deposited in the renal tract. A fluid intake sufficient to maintain a daily urinary output of at least 1,500 c.cm. has been recognized as a valuable measure in the avoidance of crystalluria, whatever sulphonamide is being given. The observations of Jensen and Fox seem to provide a clear indication for the use of alkali as an adjuvant to sulphathiazole or sulphadiazine therapy, not only to eliminate the risk of crystalluria but to increase their therapeutic efficacy in the urinary tract. Large doses of alkali are required to neutralize the usual acidity of the urine and also that of the sulphonamide. Gilligan and her colleagues recommend divided doses every four hours to maintain a relatively constant

urinary pH throughout the day and night. The reaction of the urine should be tested with litmus paper and the alkali must be continued for twenty-four hours after the sulphonamide has been stopped. The daily amount of alkali recommended is gr. 240 of sodium bicarbonate, gr. 320 of sodium lactate or gr. 280 of sodium citrate. These large doses are said to be well tolerated and no alkalosis has been observed.

**Psychological Medicine: Current Methods of Treatment**

By I. SKOTTOWE, M.D. (Glas.), D.P.M.

(Abstracted from the *Lancet*, i, 11th March, 1944, p. 329)

**THE PSYCHIATRIC INTERVIEW**

TREATMENT starts from the moment of introduction to the patient. In this connection the importance of the correct technique of the initial psychiatric interview is great. It is a non-recurring opportunity to influence the patient, wittingly or unwittingly, for long-term good or ill. It may be considered in three stages: (a) the obtaining of preliminary data from the patient or a relative, but preferably from both; (b) examination proper which should always include a careful somatic, as well as a psychological, examination; (c) formulation of the nature of the illness to the patient and his relative, jointly or severally, according to what the findings may have been.

The patient's view of his illness is usually very different from the doctor's. What appears to the latter as an annoying hypochondria, or a frank delusion or an unfounded fear of cancer or insanity, or even as mere laziness and lack of effort is usually a real pressing and distressing burden to the patient. It is idle to pooch-pooch such notions or to show by one's attitude that one does not take the patient seriously or that one regards him as being obviously alienated and as some sort of 'different person'. It is just as bad to pander to fanciful whims and requests for some special investigation or treatment such as x-ray or electrical treatment, of which the patient has probably read some highly coloured account in the lay press.

Most patients feel that they are misunderstood. What is needed is to convey to the patient the notion that the doctor is there to hear his story and above all to help him. In order to do this it is essential



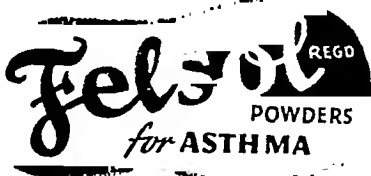
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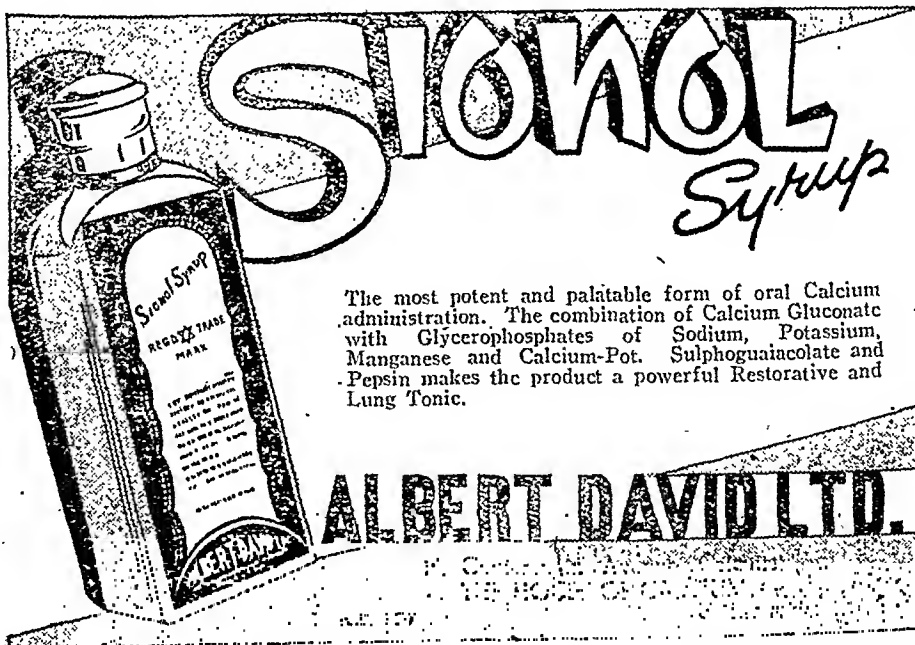
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to get out the facts and to reach a reasonable decision on them, both as to further investigation and as to the treatment to be adopted. This cannot be done in a hurry; it takes, on the average, about three-quarters of an hour; but it saves a lot of time in the long run to make a proper job of it the first time. Few psychiatric cases lend themselves to spot diagnosis; but even if the doctor sees, or thinks he can see, what the diagnosis is long before the interview is ended he must still make a thorough examination. Not only must it be thorough, but it must manifestly appear to be thorough. Nothing else will avoid serious mistakes and nothing else will convince the patient that he is in fact being taken seriously and that the future management of his case rests upon sound foundations. In the great majority of instances it will be possible at the conclusion of the initial interview to decide whether the case is predominantly a somatic disease with psychological accompaniments, or predominantly a psychological disturbance without somatic accompaniments, or with such accompaniments themselves resultant upon the psychological disturbances or otherwise. The false approach of trying to decide whether a case is functional or organic should be abandoned. Few cases are exclusively one or the other, many are both; and as a rule it is a question of deciding not 'Is it this or is it that?' but 'How much is it this and how much is it that and what is the relationship between the two?'

A decision on this point must be reached as soon as possible. Special investigations should be undertaken only if there are sound grounds for doing so, never simply for their own sake, or because the patient demands them. To yield to such tempting and imposing evasions results only in perpetuating faulty conception of his illness in the patient's mind; and sooner or later it will occur to the more intelligent patient that a doctor who subjects him for many weeks to expensive investigations, and at the end of it all can report only that there is no evidence of this or that, cannot be very sure of his ground, and is not doing much to make a constructive and helpful diagnosis or a reasonable plan of treatment. Extended investigation and so-called 'observation' has been seriously overplayed in psychiatry. The categorization of a case as 'functional'—if one must adhere to ancient dualistic conceptions—should never rest exclusively upon the absence of organic signs; and a functional aspect of the illness should never be excluded merely because of their presence. It should be remembered that functional symptoms have a positive aetiology, and until it is found it is unwise so to designate any illness; and furthermore that an organically determined symptom—for instance, sciatic pain—may be dealt with in a neurotic way. All along it is essential not only to treat any organic disease that may be present but also to treat, manage and cope with the patient as a person.

A simple but unequivocal formulation of the nature of the illness can be conveyed to the patient by pointing out that he is a person as well as a collection of organs, that his feelings and thoughts emerge from the way he is constituted and from the experiences which he has undergone, that they can be modified not only by changes in his organs but also by changes in his way of living; and that they can themselves produce bodily changes such as palpitation, clammy hands, tense muscles with a consequent sense of fatigue or breathlessness (remembering the diaphragm), uncomfortable abdominal sensations and so on; and furthermore that personal feelings and thoughts can perpetuate and utilize organic disabilities for the satisfaction of personal aims. In this way the patient can be persuaded that changes in, and sensations apparently located in, various organs do not necessarily imply disease of the organ in question; the presence or absence of the latter is decided more reliably by medical examination than by the patient's own interpretation of his symptoms.

He should be made to feel that his illness is not some mysterious and unique visitation but is in fact

something well understood, of which numerous examples are seen in other patients. The therapeutic value of a factual explanation of the illness, of rational persuasion in respect of symptoms and of clear-headed decisiveness instead of woolly ramblings about further investigation, is very great indeed, and in fact it forms the foundation of the future psychological management of the case; so much so that in outpatient practice it is found that protracted and repeated psychotherapeutic interviews need not take place in most cases if the initial interview has been properly handled, subsequent interviews being concerned more with practical problems in the patient's way of living (reinforced by visits from a competent social worker) and with brief reassurances or explanations.

#### DISPOSAL

In perhaps a sixth of the cases seen in outpatient practice it will be obvious that the patient must be admitted to a mental hospital. The main indications for this are: actual or potential disorders of conduct; the manifest presence of a serious disorder such as schizophrenia; advanced affective disorders like fully established melancholia or mania; and serious organic psychoses with florid confusional, delusional or hallucinatory episodes for which adequate treatment cannot be had elsewhere. A mental hospital should not be regarded as a last resort in disposal, but as a place which provides essential treatment for certain forms and degrees of illness. The decision whether or not to recommend it in the individual case can rest only on accurate diagnosis, and it should be remembered that a denial of mental hospital admission may also be a denial of the only plan of treatment that is likely to be effective. It is, for instance, almost an act of gross negligence to pat an early schizophrenic on the back, tell him he is suffering from a 'nervous breakdown', give him a bottle of bromide and send him for a seaside holiday at the very phase of illness in which mental hospital treatment is likely to be most effective.

But about 80 per cent of psychiatric cases do not require mental hospital treatment, and some would be made frankly worse by it. This large group is made up predominantly of mild affective disorders, usually depressions and anxiety states, and mild organic syndromes with irritability, fatigue, tearfulness and failure of sustained mental effort as their leading features. In addition there will be some obsessional states, some conversion hysterics and a fair number of constitutional anomalies such as high-grade defect and psychopathic personality. These latter anomalies should always be suspected if there has been a poor school record, frequent changes of employment, abscondings from home, more than one illegitimate pregnancy, trouble with the police and repetition of petty crime, or the 'persistent' spending of substantial sums of money with nothing to show for it.

A rough-and-ready help in diagnosis and consequently in disposal is the application of a quick verbal and a quick performance test. In practice, Burt's reading test and the proteous mazes can be applied in about five minutes. Together with the history they will give a reasonably reliable clue to the development of the patient's native intelligence and to his scholastic attainment. In young people, if the two tests rate the patient at the same mental age, and if it is 12 years or less (i.e. 2 years below average adult) high-grade defect may be suspected and more extended examination of the intellectual status should be carried out. If the test scores show pronounced scatter (failure in some simple tests but success in more difficult ones) an emotional or toxic factor is probably of more immediate importance than the constitutional state. If there is a discrepancy of more than 2 years of mental age between verbal and non-verbal tests in favour of the latter, one should suspect the presence of a special disability, especially if the patient be left-handed or left-eyed, and one begins to contemplate disposal in terms of the services of an educational psychologist; if the discrepancy is in favour of good verbal performance one may suspect either defectiveness or a psycho-



pathy, and the question of disposal in terms of occupational selection and social service supervision begins to be more prominent.

I mention these slight degrees of constitutional anomalies because they are often masked by and indeed may be the main causal factor in many neurotic syndromes and behaviour problems, and because they are so easily overlooked if one does not happen to think of them. To attempt to treat a neurotic syndrome by, for example, exclusively psychotherapeutic means is a sheer waste of time if the main underlying factor is a constitutional anomaly of the defective or psychopathic type. Such illnesses can only be dealt with by careful investigation, readjustment and continued supervision of the patient's social circumstances, including domestic as well as occupational adjustment. This is an indispensable aspect of treatment not only in constitutional anomalies but in some 30-50 per cent of all psychiatric cases. To be effective it requires a carefully set up organization with wide social contacts, and a staff of properly trained psychiatric social workers. Rapid advances are being made in this way not only within the framework of voluntary hospital and local authority social services but also on a wider and more ambitious scale by the Provisional National Council for Mental Health, which is among other things a kind of integrating machinery for psychiatric social service on a nation-wide scale.

Having filtered off the group of prospective mental hospital admissions and that of disabling though slight constitutional anomalies, there remains a large group of illness, mainly of affective or mild toxic exhaustive type; essentially recent illnesses in previously healthy people to whom something has happened; illnesses in which the accent is on environmental rather than constitutional factors, though the latter are still present. Many of these patients will have had previous attacks of a similar kind of illness or will be found to display personality traits which are associated with liability to such illness; but the main point is that at the somatic, the psychological or the social level there has been an impact with some disturbing and probably modifiable or remediable factor.

A small proportion of these will require impatient treatment in a general hospital, or in a psychiatric ward or unit of such a hospital or in a neurosis centre. The main indications for such admission rest upon the need for applying special methods of treatment—for instance, lengthy narcosis, narco-analysis and shock treatment which cannot or should not, in my view, be attempted under outpatient or domiciliary conditions. But it is also indicated in cases otherwise suitable for outpatient treatment where the social circumstances are so adverse as to stultify such treatment—for instance, in the case of homeless people living in lodgings or hostels, or elderly people living alone, not getting proper food and warmth and so on, or where the illness has emerged from some domestic crisis from which it is essential that the patient should have a break.

#### DOMICILIARY AND OUTPATIENT TREATMENT

There remains, however, a substantial majority of psychiatric patients who can be treated under domiciliary conditions with or without attendance at a psychiatric outpatient department.

The main methods of treatment are :

(a) To persuade the patient, relatives and employers to accept the facts of the illness for what they are and to adopt a rational attitude towards it.

(b) To prescribe a practical daily life: by deciding, for instance, whether the patient is to continue at work or not; if so, whether on full-time or part-time, and with what occupational adjustments; or if he is to stop work, what he is to do: is he to be in bed, or up, or up part of the day? To look into the possibilities of congenial remedial occupation at home. What are his hobbies? Is company to be encouraged or not? Who is there in the house with him, is he to get away to some other relatives for a time, or if in lodgings is he to go home? Advice should be given to relatives on elementary anti-suicide precautions. The most likely

time for such urges to appear is in the early mornings. Removal of opportunity is the main step.

(c) To attend to somatic functions. Is his diet adequate? What of his fluid intake? Exercise, bowels and sleep all require consideration. Are there any minor maladies—e.g. dental sepsis, sinusitis, or minor degrees of malnutrition which require correction? Vitamin additions, especially the whole B-complex, are often valuable.

(d) To relieve symptoms, such as anxiety with excessive visceral responsiveness, depression and tearfulness, insomnia. A sound prescription for this is tincture of opium, minims 12 to 15, with minims 7 to 10 of liquid extract of cascara, made up with chloroform water, taken well diluted three or even four times daily. It is effective; I have never seen it produce an addiction; and it is unpleasant to take and the patient is not likely to hoard it and take an overdose, as may easily happen with barbiturates, especially in tablet form.

(e) Psychiatric interviews, which should deal with practical problems in the patient's life. They should be short, frank, reassuring and externalizing rather than introspectionist.

(f) To use the services of a social worker, who will assess the social situation objectively, see that treatment is properly carried out and that the patient gets a square deal in the numerous and irritating ramifications of such problems as allowances, insurance, security of future employment and so on.

A plan of treatment on these lines is effective in some 60 per cent of minor psychiatric disorders. If they are not dealt with promptly and effectively in this way, some of them become worse and require hospital admission, many drift into chronicity and go to swell the ranks of those reproaches to outpatient practice, the weekly bromide-toppers. Bromide is a much more dangerous drug than is commonly supposed, for it produces chronic intoxication with lethargy, irritability and confusion if continued indefinitely.

#### SPECIAL METHODS OF TREATMENT

Some of the more prominent special methods of treatment applicable to hospital inpatients may be briefly considered.

(a) *Continuous narcosis*.—This is indicated when emotional distress is intolerable, faulty ways of thinking are tending to become habitual, sleeplessness is severe and exhaustion is becoming manifest. It is contra-indicated by renal disease and acute respiratory infections. There are several methods of applying it, but barbitone by the mouth has proved most effective. Toxicity is controlled by insulin, glucose and fluids. Narcosis is maintained for 12 to 14 days. It is a rational treatment because it secures rest for the affected part—the mind—it induces a pleasant affective state, breaks a vicious circle, and renders the patient amenable to suggestion and persuasion. It is nowadays almost devoid of risk. In acute panic states, narcosis is best induced rapidly, in a matter of minutes, by intravenous barbiturates and thereafter continued by intramuscular or oral administration.

(b) *Narco-analysis*.—This may be used for diagnostic or therapeutic purposes or both. In essence it consists in inducing a dissociated, disinhibited state by the rapid means of intravenous injection or barbiturates like sodium amytal. It is useful for bringing to the surface relevant psychological material which the patient, wittingly or otherwise, will not produce when he is fully conscious; but its greatest advantage is in relieving the muscular tension or tremors or paralytic symptoms of a conversion hysteria of sudden onset, or for relieving a hysterical amnesia. It resembles, and is to some extent a substitute for, hypnosis, but it does not imply the personal rapport which hypnosis requires.

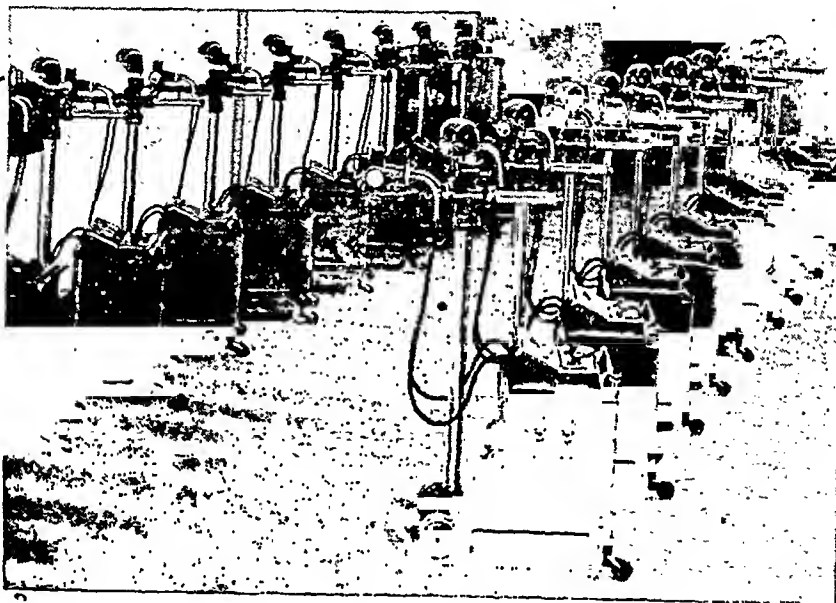
(c) *Shock therapy*.—This popular title is a misnomer: a state of shock should not be allowed to develop. It refers to: (1) repeated hypoglycaemic comas lasting 45 to 90 minutes induced by gradually increasing doses of insulin, and relieved on each occasion by glucose

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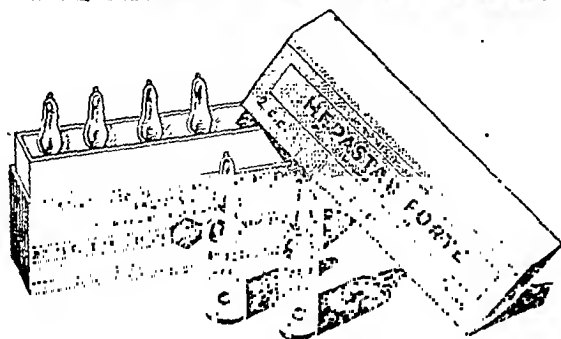
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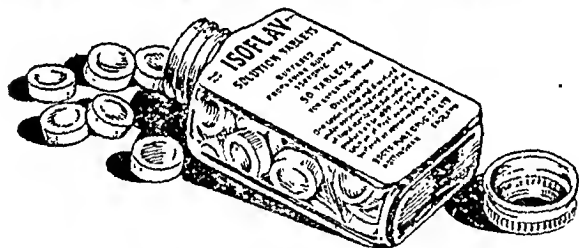
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intravenously or by the nasal tube, some 40 to 60 comas constituting a course of treatment; (2) convulsions induced by analeptic drugs like leptazol or by passing an electric current across the skull (between 10 and 15 convulsions are induced with about a 3-day interval between each). There is nothing to choose between the effectiveness of the two convulsive methods and neither is more frightening nor more dangerous than the other if the technique is correct. Neither insulin comas nor induced convulsions are free from danger, and they have a definite mortality risk, although it is only one in many hundreds. Induced convulsions occasionally produce fractures and dislocations, not only of limbs but even of the vertebral column though lasting paraplegia is extremely rare. Both forms of treatment are contra-indicated by the presence of tuberculosis and myocardial disease. Neither will cure schizophrenia although both will abate the florid symptoms like delusions, hallucinations and oddities of conduct; the fundamental hall-marks of the condition—*affective flattening and disorder of the thinking process*—remain.

Affective disorders of retarded depressive type, and stupors, do well with induced convulsions and in such illnesses the sooner they can be applied the better. Sometimes a preliminary continuous narcosis can be used with advantage to relieve distress. Patients with motor restlessness, loss of weight and toxic-exhaustive manifestations do better with insulin comas. The indiscriminate use of induced convulsions merely because it is easy to do and is sometimes dramatic is to be severely deprecated. The *modus operandi* of all these treatments is not precisely known. It is certainly connected with the carbohydrate-oxygen metabolism of the nervous system and possibly with endocrine-hypothalamic-autonomic functions. Inasmuch as some psychiatric illnesses sometimes show evidence of disturbance of these functions such treatments may sometimes be rational; but more often they are empirical.

(d) *Prefrontal leucotomy*.—This is another treatment that is liable to be recommended blindly or because all else has failed. Occasionally it succeeds in chronic cases that have failed to respond to induced convulsions. It consists in cutting parts of the white matter between the frontal cortex and the basal ganglia; and if it has a rational basis it would appear to be that by severing cortico-basal association fibres it breaks the supposed neurological substrate of the linkage between particular emotions and particular perceptual contents. Thus it may relieve the automatically reiterated depressive symptoms of the chronic involutional agitated depression. It has also been reported to relieve the gross behaviour disorders and noisiness of chronic psychotic epileptics and paraphrenics. There is insufficient evidence yet to justify its widespread application to any particular form of recent, acute psychiatric illness, but it has produced some excellent results in apparently very chronic cases, quite inexplicable, and also some disappointing failures. A good initial personality and helpful relatives are essential *pre- and post-hoc* influences respectively.

It does not impair intelligence, though it may diminish the sparkle and spontaneity and capacity for abstract, conceptual thinking of the patient. The mortality risk is small but definite and the operation should, of course, be undertaken only in the field of activity of a specialized neurosurgical team.

(e) *Psychotherapy*.—The various forms of psychotherapy which can be grouped into two main divisions—the rational persuasionist and the analytical—continue to be indispensable. It has been well said that the therapist matters more than the therapy, for the end-results of all forms are remarkably similar. There is little doubt that selection of method depends more on the personal proclivities of the patient and therapist respectively than on any scientific data. An interesting development is group-psychotherapy in which a series of about 12 explanatory lectures and seminars is given to a group of patients suffering from similar forms of illness—for instance, anxiety with effort syndrome—in

which explanations and persuasion are likely to be of value.

(f) *Occupational therapy*.—In the fullest sense of the term, and not only in the restricted sense of handicrafts, occupation graduated, controlled and prescribed as carefully as one would prescribe a drug is essential at some stage in the treatment of most cases. War has embarrassed the development of the handicraft side, but has accentuated the value of occupational selection and guidance in the light of more realistic experimental psychological tests than have been hitherto considered valuable in the clinical field.

## The Biosynthesis of Thiamine in Man and Its Implications in Human Nutrition

By V. A. NAJJAR, M.D.

and

L. E. HOLT, M.D.

(From the *Journal of the American Medical Association*, Vol. CXXIII, 13th November, 1943, p. 683)

THE thiamine requirements of man are not known with accuracy. The daily allowances recommended by the National Research Council's committee on medical nutrition were based on three experimental studies of induced thiamine deficiency in human volunteers which did not show very close agreement in regard to the minimal requirement. The difficulty encountered in experiments of this kind, one which we have experienced ourselves, is the great variation in the thiamine content of natural foods, making it next to impossible to maintain a constant intake when such foods are given. In order to avoid this difficulty and to control thiamine intake accurately we undertook experiments on a synthetic diet in which vitamins were supplied exclusively by a vitamin mixture given with each meal in weighed amounts.

The subjects of this study consisted of 9 adolescent young adult males from 16 to 23 years of age, living a sedentary life in an institution. Their diet, which was furnished in quantities approximating 40 calories per kilogram, consisted of vitamin-free casein, crisco, dextrimaltose, a mineral mixture and a vitamin mixture. The food was mixed together to form a somewhat granular dough, which was given in equal quantities at each of the three meals. The subjects soon became accustomed to this food and ate it with every appearance of relish. In all, this monotonous regimen has been continued for eighteen months during which time weight and vigour have been maintained.

The plan of the experiment was to vary only the thiamine intake, reducing this very gradually from an initial level of 1 mg. per day in order to ascertain the minimum thiamine intake that would prevent thiamine deficiency. The subjects were given periodic physical examinations; their blood and urine were examined routinely. Electrocardiograms were taken from time to time, and occasional roentgen observations were made on the motility of the gastrointestinal tract. The thiamine excretion in the urine was followed daily, using the 'fasting hour' excretion test described by us, occasional observations were also made on the twenty-four hour urinary excretion of thiamine and on the blood pyruvate.

### RESULTS

During the course of many months the thiamine intake was gradually reduced without encountering any clinical or laboratory evidence of thiamine deficiency. Thiamine excretion in the urine fell to negligible figures when the intake was reduced to 0.4 to 0.6 mg. per day. By the ordinary thiochrome procedure zero thiamine values were commonly found, but by a more sensitive modification developed by one of us it was possible to demonstrate that quantities up to 2 or 3 micrograms per hour and from 15 to 25 micrograms a day were still excreted in the urine. With further reductions in the thiamine intake no further decrease in

urinary thiamine was observed. Eventually, when the subjects had remained on thiamine intakes between 0.1 and 0.2 mg. per day for months, thiamine was omitted altogether from the diet. In the course of the next three to five weeks, 4 of the 9 subjects developed definite clinical evidence of thiamine deficiency (neuritis or oedema, in association with anorexia and sometimes vomiting); 1 other subject developed questionable evidence (anorexia and vomiting only) and the remaining 4 subjects showed no signs of deficiency during a seven weeks' period of observation.

TABLE 1.—Output of free and combined thiamine in faeces of patients on a completely thiamine-free diet (Figures represent micrograms excreted per day, an average of periods of one week's duration)

Subject	Symptoms of thiamine deficiency	THIAMINE IN FAECES			
		Period 1		Period 2	
		Free thiamine	Combined thiamine*	Free thiamine	Combined thiamine.
C. G.	Present	9.8	152	8.5	22.4
H. K.	"	5.0	0	4.5	0
A. P.	"	4.7	111	5.5	0
R. A.	"	11.5	73	15.6	36
S. B.	Questionable	26.0	217	..	..
C. P.	Absent	250	40	507	129
G. B.	"	52	125	37	19
D. K.	"	143	8	182	25
J. S.	"	53	58	43	201

\*Indicates thiamine liberated by treatment with clarase.

Since it seemed likely that the reserves of thiamine had been greatly depleted by the prolonged period of low intake even before the completely thiamine-free regimen was instituted, it would have been anticipated that none of these subjects could withstand complete withdrawal for more than a few weeks. An explanation was therefore sought for the failure of the remaining 4 subjects to develop deficiency. Repeated examination of the diet failed to show any trace of thiamine; examination of the stools, however, provided very illuminating information. It was found that the 4 subjects who had developed deficiency had almost no free thiamine in their stools. A somewhat larger amount of free thiamine was present in the subject whose symptoms were questionable, whereas each of the subjects who remained free of symptoms had large quantities of free thiamine in the faeces (table 1).

#### COMMENT

It will be noted that the stools of most of the subjects contained considerable amounts of combined thiamine in some combination that yielded free thiamine on treatment with clarase. However, the close correlation between the symptoms and the low value of free thiamine and the lack of correlation between the symptoms and the combined thiamine suggests that the latter may be in a form unavailable to the body. The source of the thiamine in the faeces remained to be explained.

Two possibilities to be considered were (1) that intestinal bacteria were manufacturing thiamine, a phenomenon that is known to occur in the rat under certain conditions and in the rumen of certain ruminant animals; (2) that the stores of thiamine in the body had not been completely exhausted and that the

faecal thiamine represented an excretion into the intestine. The latter alternative seemed rather unlikely in view of the fact that urinary thiamine excretion had for many months remained at extremely minute levels. The possibility of thiamine excretion into the intestine was tested by administering 50 mg. of thiamine intravenously to 1 subject daily for one week in order to find out whether this was followed by an increased thiamine content of the stools. A negative result was obtained.

In order to obtain direct evidence for the production of thiamine by the intestinal bacteria, one of the symptom-free subjects (G. B.) was given succinylsulfathiazole by mouth 1.5 gm. every four hours for one week. The faeces of this subject showed a prompt reduction in free thiamine; from the previous values of 37 and 52 micrograms per day it fell within a week to zero, reappearing a few days after the drug was discontinued. Conceivably this negative result may have been due to direct destruction of thiamine by succinylsulfathiazole or to some interfering effect of the drug on the thiamine determination. Both these possibilities have been explored and ruled out. It is thus clear that the thiamine in the faeces had its origin in the intestinal bacteria.

It is conceivable that the faecal thiamine was formed only by bacteria present in the large intestine, a site from which absorption of thiamine is perhaps impossible.

TABLE 2.—Urinary excretion of thiamine following administration of thiamine by enema (Micrograms in twelve-hour specimen)

Subject	Before thiamine enema	After two thiamine enemas
A	160	1,615
B	162	5,200

If this were the case, the presence of faecal thiamine would not explain the protection from the deficiency which these 4 subjects exhibited. In order to test this possibility, retention enemas containing 50 mg. of thiamine were given to 2 persons on successive days. Twelve-hour collections of urine were made before this regimen was started (control period) and on the day the second enema was given. The results (shown in table 2) indicate a pronounced rise in urinary thiamine as the result of the thiamine enemas and provide ample proof that the large intestine can absorb thiamine.

It is not possible to state at the present time that thiamine requirements can be sustained for an indefinite length of time by such thiamine as is formed by intestinal bacteria. It may be that minute amounts of oral thiamine are needed for the growth of the bacteria which synthesize thiamine. The nature of the organisms which synthesize thiamine and the relation of diet to such bacterial synthesis are now under investigation.

The demonstration that intestinal bacteria can synthesize thiamine carries interesting implications for human nutrition. This phenomenon may explain the discrepancies in thiamine requirements found by different observers. Since it is likely that the biosynthesis of thiamine is greatly affected by diet, as is known to be the case in animals, it follows that we must think in terms of requirements on particular diets rather than of requirements in general. It is quite possible that dietary factors other than the thiamine content may explain in part some of the paradoxes in the incidence of beriberi. The possibility of controlling thiamine deficiency by means other than thiamine administration remains to be explored. Finally, we may point out that the inhibition of the biosynthesis of thiamine by a sulfonamide drug has an important clinical implication for the physician who uses these drugs.

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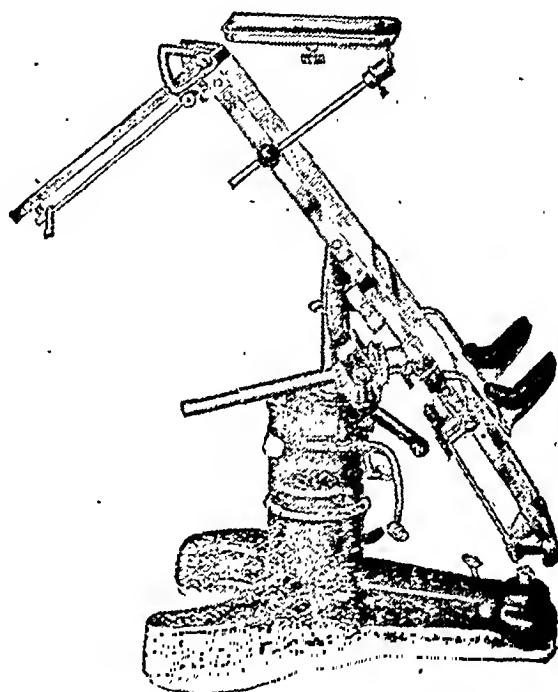
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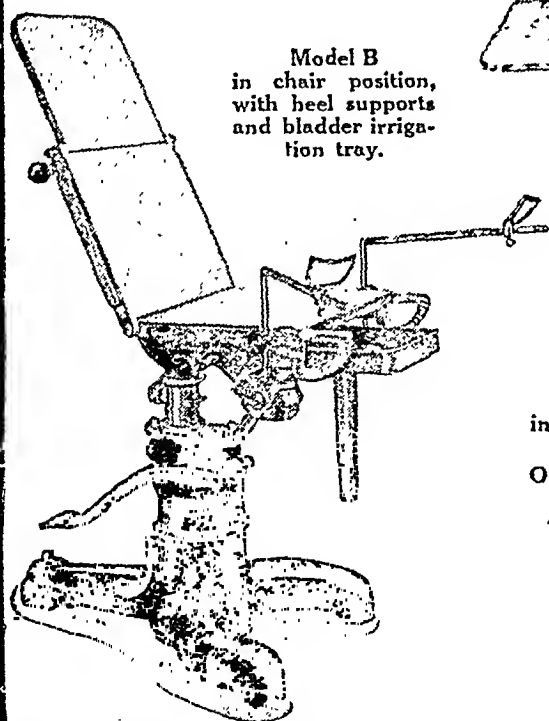
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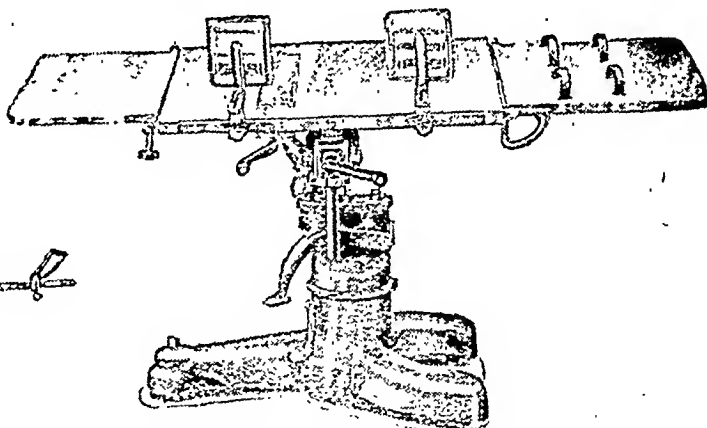
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## Reviews

**MASS MINIATURE RADIOGRAPHY: A PRACTICAL HANDBOOK.**—By R. R. Trall, M.C., M.A., M.D., F.R.C.P., H. J. Trenchard, M.B., Ch.B., M.R.C.P., and J. A. Kennedy, M.B., B.S., M.R.C.S., L.R.C.P. 1943. J. and A. Churchill, Limited, London. Pp. viii plus 96. Illustrated. Price, 8s. 6d.

THIS little book has been produced as a practical guide to the setting up and running of a Mass Miniature Radiography Department.

The method, first introduced by de Abreu in 1936, consists of the photographing of the image on a fluorescent screen on to a photographic film, and was made possible by improvements in recent years in fluorescent screen and lens manufacture.

The type of film recommended is the 35 mm. film used by the U. S. Navy, Royal Navy and Royal Air Force. As many as 100 to 120 persons an hour can thus be passed under radiographic survey of the chest. As pointed out in the foreword by Lord Dawson of Penn, the method affords valuable statistical information concerning the nation's health by the detection of unsuspected cases of tuberculosis of the lungs, who would then be referred to their own doctors or tuberculosis dispensaries for further investigation and treatment.

The book deals with the administration, building, equipment, staff and interpretation of miniature films together with the correlation of results which should precede diagnosis and disposal.

The style is eminently clear and practical, and the book should prove of great value to those interested in this effort to link up the X-Ray Department with the progress of medicine and the welfare of the community.

J. A. S.

**WAR TIME ECONOMY IN PRESCRIBING.**—By J. R. Goyal, M.B., B.S. 1944. Published by the author. Printed by the Alblon Press, Kashmere Gate, Delhi. Pp. viii plus 184. Price, Rs. 6

THE author starts by telling us how to economize in aqua distillata, alcohol, glycerine, oils and fats, etc. But by far the greater part of the book is devoted to giving lists of proprietary medicines, foreign and Indian, of established as well as doubtful reputation. For malaria the author rightly recommends quinine, mepacrine and plasmochin, but what was the idea in giving a list of injectable preparations containing iron or arsenic with quinine and which may be selling at fancy prices? He says that vitamins are best administered in the form of foodstuffs and then gives a list of about 120 preparations of which the majority come from foreign countries. And so with the drugs for tuberculosis, hormone products, etc. Where does economy come in?

R. N. C.

**FOOD INSPECTION NOTES: A HANDBOOK FOR STUDENTS.**—By H. Hill, F.R.San.I., F.S.I.A., A.M.I.S.E., and E. Dodsworth, M.R.San.I., M.S.I.A. 1943. H. K. Lewis and Company, Limited, London. Pp. vii plus 121. Price, 6s.

THIS pocket book contains much information about foods and their inspection. It does not claim to be a textbook, but gives a summary of our present-day knowledge of the subject which will be helpful to public health students in revision for examination and to public health officers for ready reference in their daily routine work. Nearly half the book is devoted to meat inspection, and the remainder deals with poultry, rabbits and game, fish, milk and milk products, etc. There is a short chapter on food poisoning towards the end.

R. N. C.

**PASTEURIZATION.**—By Harry Hill, F.R.San.I., A.M.I.S.E., F.S.I.A. 1943. H. K. Lewis and Company, Limited, London. Pp. viii plus 152. Price, 10s.

PASTEURIZATION is still in its infancy in India, the vast majority of the people being content with boiled milk which, in spite of its keeping qualities and distinct flavour, suffers from the disadvantage of having lost some of its nutritive value owing to excessive heating. In cities, where the milk supply is at present in very unsatisfactory state, the demand for pasteurized milk is growing, and it is probable that this demand will increase in future. The process aims at destroying harmful organisms, while retaining the nutritive value of milk. Those who desire enlightenment on the subject will find Mr. Hill's book very practical. In the first three chapters, he discusses the necessity for pasteurization and answers the criticisms of those who oppose it, for it must be remembered that in England there are still people who for various reasons are against the method of treating milk. He rightly insists that pasteurization is not a substitute for clean milk, that it does not render dirty milk clean, and that milk possessing a high bacterial content cannot be efficiently pasteurized; in other words, a certain standard of cleanliness is essential for production of raw milk before it is processed. In the subsequent chapters he gives a clear account of plant design, various processing methods and control measures, not forgetting minor matters such as washing and sterilization of milk bottles and cans, adequate sealing, etc. All interested in the production of clean milk should read this book.

R. N. C.

### BOOKS RECEIVED

1. The permeability of natural membranes. H. Davson and J. Frederic Danielli. Published by Cambridge University Press. Price 25s.
2. A new conception of kerato-conjunctivitis sicca. H. Sjogren. Set up and printed in Australia by the Australasian Medical Publishing Company, Limited, Glebe, New South Wales. Price not stated.
3. The natural development of the child. Second edition. Agatha H. Bowley. Published by E. and S. Livingstone, Edinburgh. Price 8s. 6d. Postage 5d.
4. Skin grafting of burns. James B. Brown and Frank McDowell. Published by J. B. Lippincott Company, Philadelphia and London. Price not stated.
5. Annual review of biochemical and allied research in India. Volume XIII for 1942. Published by the Society of Biological Chemists, India, Malleswaram, Bangalore. Price Rs. 3.
6. Rose and Carless' Manual of Surgery for students and practitioners. C. P. G. Wakeley and J. B. Hunter. Seventeenth edition. Volumes I and II. Published by Baillière, Tindall and Cox, London. Price, 35s.
7. Principles of Unani medicine. Hakim Ahmed Husain. Published by S. Husain, 7, Perumal Chetty Street, Vepery, Madras. Price Rs. 3.
8. Surgical Nursing and After-treatment. Eighth edition. H. C. Rutherford Darling. Published by J. and A. Churchill Limited, London. Price 12s. 6d.
9. Surgery of Modern Warfare, edited by H. Bailey. Parts I, II, III, IV, and V. (To be complete in six parts.) Third edition. Published by E. and S. Livingstone, Edinburgh. Price 15s. and postage 6d. for each part.
10. The Queen Charlotte's Textbook of Obstetrics. L. C. Rivett, L. Phillips, G. F. Gibberd, A. C. H. Bell, D. Macleod, W. R. Winterton and H. G. E. Arthure. Sixth edition. Published by J. and A. Churchill Limited, London. Price 25s.
11. The vascular abnormalities and tumours of the spinal cord and its membranes. R. Wyburn-Mason. Published by Henry Kimpton, London. Price 18s.
12. Venereal diseases. (Catechism series.) Second edition. A. Cameron Ewing. Published by E. and S. Livingstone, Edinburgh. Price 1s. 6d. Postage 3d.

13. Mental diseases. (Catechism series.) Third edition. Published by E. and S. Livingstone, Edinburgh. Price 1s. 6d. Postage 3d.

14. Public health. Parts I and II. Fourth edition. (Catechism series.) Published by E. and S. Livingstone, Edinburgh. Price 1s. 6d. and postage 3d. for each part.

15. Physiology. Part I. Fifth edition. (Catechism series.) Published by E. and S. Livingstone, Edinburgh. Price 1s. 6d. Postage 3d.

17. Diseases of the eye. Fourth edition. (Catechism series.) Published by E. and S. Livingstone, Edinburgh. Price 1s. 6d. Postage 3d.

18. Massage and remedial exercises in medical and surgical conditions. Sixth edition. N. M. Tidy. Published by John Wright and Sons Limited, Bristol. Price 25s.

19. Vade mecum of medical treatment. W. Gordon Sears. Fourth edition. Published by Edward Arnold and Company, London. Price 10s. 6d.

20. The diabetic life. Thirteenth edition. R. D. Lawrence. Published by J. and A. Churchill Limited, London. Price 10s. 6d.

21. Medical Research Council, special report series no. 248. *A provisional classification of diseases and injuries for use in compiling morbidity statistics.* Published by His Majesty's Stationery Office, London. Pp. 168. Price 3s.

22. The radiology of bones and joints. Third edition. J. F. Brailsford. Published by J. and A. Churchill Limited, London. Price 45s.

23. The British encyclopædia of medical practice; medical progress, 1943 and cumulative supplement, 1943, edited by Sir H. Rolleston. Published by Butterworth and Company (Publishers), Limited, London. Price not stated.

## Abstracts from Reports

### REPORT ON THE WORK OF THE LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE (UNIVERSITY OF LONDON) INCORPORATING THE ROSS INSTITUTE FOR THE YEAR 1942-43

COLONEL G. S. PARKINSON, the acting Dean of the School, having taken up a war appointment overseas, Professor M. Greenwood is at present in administrative charge of the School. As the normal classes have been suspended for the period of the war, teaching has been confined to short courses in tropical medicine and parasitology for Army medical officers. During the year under review, 14 courses were held and were attended by 921 officers. Various other short courses were also provided. In spite of difficult times, research activities were continued but on a limited scale. Dr. V. B. Wigglesworth has been appointed director of a unit on Insect Physiology under the Agriculture Research Council. Miss Young has completed her study of the helminths of sub-clinical importance and of protozoal infections in school children. She has also studied *Trichinella* infections in England. Dr. Buckley has continued his investigations on *Onchocerciasis* in the gold-fields of East Africa. Mr. David under a grant from the Medical Research Council continues to study insecticides and Mr. Robinson is working on the difficult problem of killing *Ornithodoros moubata*, a tick which transmits relapsing fever. Among the other activities, was the study on *Penicillium patulum* (patulin) which shows some promise in the treatment of the common cold. Sir Malcolm Watson retired from the Directorship of the Ross Institute at the end of 1942. The Institute has continued its activities, though work overseas is naturally curtailed at present. Professor Buxton was elected a Fellow of the Royal Society. The staff of the School have rendered much direct assistance to the services and the government departments engaged in urgent work of national importance.

## Correspondence

### INTESTINAL FLORA AND NUTRITION

SIR,—There is one aspect of study in nutrition which does not yet appear to have been accorded its true value. I refer to the part played by the organisms living inside the alimentary tract of man. To the majority studies on nutrition end at the stage at which the food is swallowed. Others, more exact, define conditions in which absorption of the ultimate products of digestion is disturbed as follows:—

(1) By mechanical causes such as short circuits, internal fistulae, obstruction of the lumen or excisions of gut or irritative conditions causing 'intestinal hurry', form one group of conditions limiting absorption.

(2) By inadequate supplies of the secretions necessary to break down foods into their ultimate constituents as in achylia gastrica, pancreatic insufficiency, and obstruction of the common duct.

(3) Those conditions where abnormalities of the absorptive mechanism exists as a primary condition in coeliac disease, ? in sprue, mesenteric lymphadenopathy or as an end result in pellagra and sprue.

(4) A miscellany of conditions in which the absence of one substance prevents the absorption of another, e.g. the interrelation of vitamin D and calcium and of bile with vitamin K, or where the excess of one precipitates or otherwise removes from the gut contents essential substances, e.g. phytic acid and calcium, or mineral oil and fat soluble vitamins. All the above, however, rest on the basic assumption that foodstuffs are digested under more or less ideal conditions by ferments strictly human in origin, and that the end products of digestion are then available for absorption dependent only on the presence or absence of the limiting factors mentioned above.

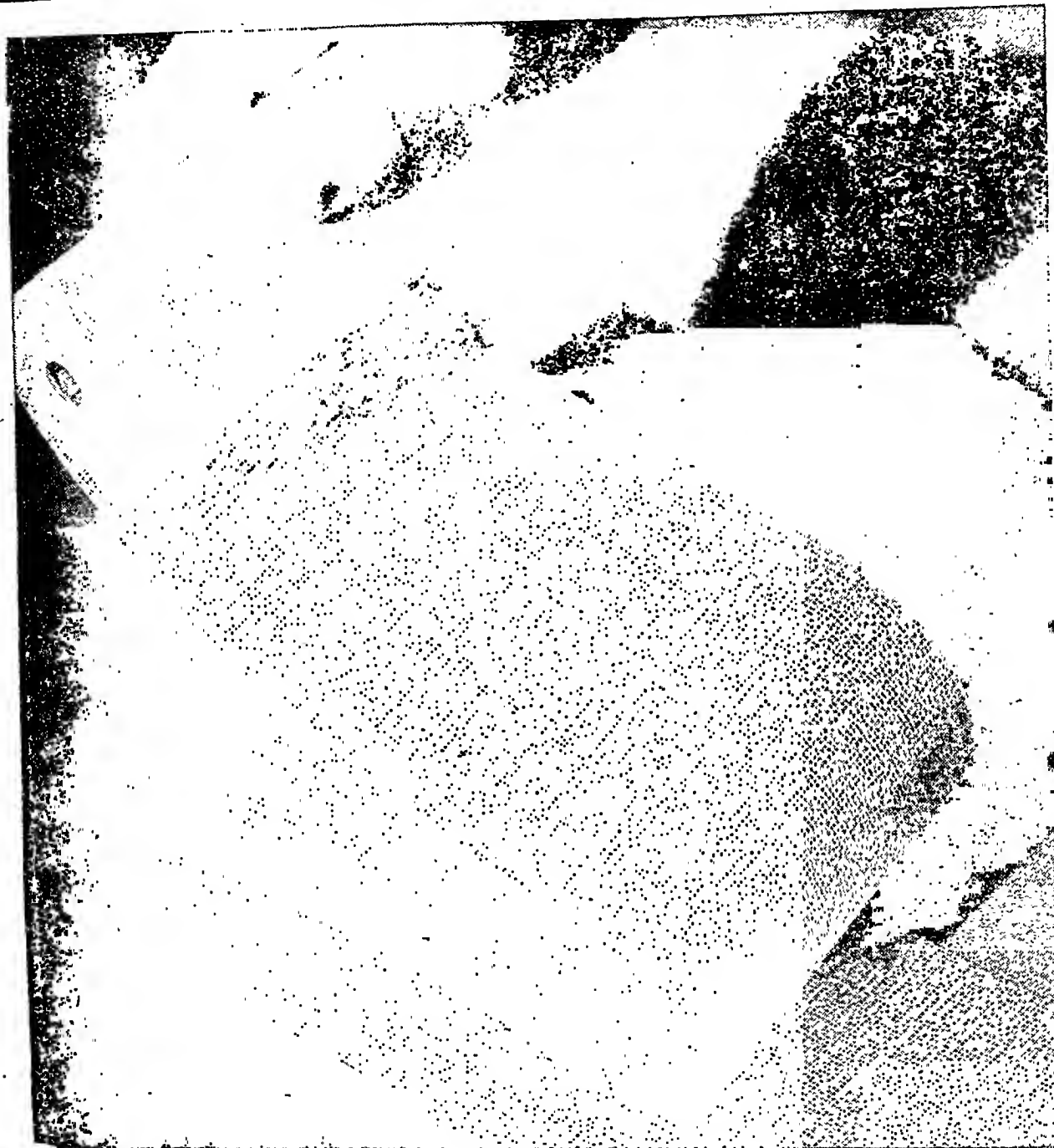
But I feel concerned to emphasize that the problem is not as simple as is stated above. The digestion of food in the alimentary canal is not a procedure conducted in a test tube, regulated by the proportions and activity of the enzymes of the intestinal canal secreted in response to chemical or psychical reflexes. *The digestion proceeds under the influence of enzymes both human and bacterial* and the end products of such a welter of enzymes may differ exceedingly from the isolated ideal digestion with pure alimentary enzymes in a test tube. It is not however simply the digestion which is influenced by the presence of bacteria, the very disposal of these end products may also be affected.

I wish to postulate that the study of nutritional deficiencies is incomplete unless the part played by intestinal organisms is also assessed, and I would suggest that there are conditions in which the character of the intestinal flora is the main factor which determines the development of, or immunity from, nutritional deficiencies.

Let us illustrate this point from knowledge which we already possess.

(i) We know that the bacteria of the intestinal tract possess the ability to act by means of enzymes on food substances leading to the breakdown of these foods to smaller molecules. In the herbivorous the cellulose splitting organisms present are possibly the most significant agents in enabling the creature to extract the essential food substances from the cells sheathed in otherwise indigestible cellulose. In man's alimentary canal also there are possibly bacterial enzymes which subserve a similar useful purpose. We must know of these and their potentialities, if they exist, for they render accessible foodstuffs otherwise rejected as unassimilable and thereby enhance the value of such foodstuffs.

(ii) We know that the bacteria present in the alimentary tract do not grow on air—they must be fed with suitable nutrient, which they must derive



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1

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therefore from food and the products of its digestion in the alimentary tract.

These substances essential to their growth include (1) amino acids and polypeptides, (2) vitamins, (3) minerals and (4) carbohydrates. If we confine the discussion only to the first two in the list of essential nutrients, we again find that much is known but not related to the problem of nutrition. (In relation to the essential amino acids one might comment that the work done in defining those which are essential is limited to work on laboratory animals with the exception of one or two, *e.g.* methionine and cysteine. We have little precise knowledge of their function in man except by analogy.)

Very few bacteria will grow in a medium free from amino acids, polypeptides or protein, and many refuse to grow well on the biologically poor proteins such as gelatine. There must therefore be competition between man and the organisms of his intestinal tract for these substances, and it must be remembered that the bacteria have first choice; man can only absorb what is left over or that which eludes the bacteria.

This is straight competition and with an adequate diet is probably not significant, but one can readily picture that when, say, certain essential amino acids are supplied in sub-optimal amounts in the diet, these, if essential also to the growth of the intestinal flora, may become absolutely inadequate to maintain the man himself in sound health.

There is also the possibility of competition resulting, not only in man's deprivation of essential amino acids, but of intoxication resulting from bacterial action on these substances, as, for instance, the effect of many organisms found in man's intestinal canal on tryptophane producing the toxic indol group, or the possible effect of the connection of methionine to cysteine producing that imbalance between the two, which leads to the production of hepatic cirrhosis.

We may legitimately inquire, therefore, how much of the hypoproteinæmia, occurring in men on a poor protein diet, is due to the unfair competition of his intestinal flora for the meagre protein his diet affords.

We must not forget however that some intestinal organisms may be responsible for *producing* essential amino acids and thus adding to the 'diet'. When we consider the vitamins, the first observation is that many bacteria require the very same vitamins for their growth as man requires. Indeed this fact is applied as a method for the quantitative assay of vitamins especially of the B complex.

It may be then possible to make a calculation expressing the vitamin requirement of the organism in man's intestinal tract.

But the situation cannot be expressed by a subtraction, for another factor also enters into the picture. This factor is the ability of some organisms in the intestinal tract to manufacture vitamins which are then absorbed by man. It has long been known that the majority of mammals, excepting the guinea-pig, the ape and man, are not suitable subjects for experiments in vitamin C deficiency because the organisms in the intestinal tract produce sufficient to supply all the needs of the animal. This phenomenon of *refection* is now proved to apply also to man in relation especially to vitamin B<sub>1</sub>, vitamin K and nicotinic acid. Men who have within their alimentary canal organisms producing these vitamins are not susceptible to dietary deficiency of these vitamins, and this must indeed account for many cases where the diet is notably deficient and yet no deficiency arises. But this refection is a vulnerable mechanism for the exhibition of sulphaguanidine or succinyl sulphathiazole may reduce or destroy the flora so that the patient becomes dependent upon the supply of vitamin in the diet.

In respect to the vitamins and amino acids necessary for man's well-being, therefore, the organisms of his intestinal tract simply subtract, subtract and intoxicate, or add to the quota available for absorption from his gut.

I repeat again that the character of the intestinal flora may be the most important single factor in certain

conditions which will decide man's immunity from, or susceptibility to, deficiency diseases.

(It might be possible to obtain very definite support for this argument from the analysis of the starving patients admitted to Calcutta hospitals recently. It is reasonably likely their diet was absolutely deficient in, say, vitamins and proteins over a long period, but how many of them developed physical signs of deficiency diseases—beriberi, pellagra, ariboflavinosis, scurvy or gross hypoproteinæmia?)

It is probably true to say that there is no such thing as a 'normal intestinal flora', but that for any single form of diet there is in health a characteristic flora which exists, not as a fixed community but as a labile population, which may vary from day to day, dependent on the diet.

Such a flora may however be disturbed by the entry of pathogens and the quota of each type may thereafter be grossly altered.

Ideally man and his intestinal organisms ought to live together in a state of *symbiosis*—mutual profit, but there is undoubtedly, as I have tried to show above, both *saprophytism*, by which the organism only gains, and a state of *parasitism* in which man definitely suffers. This latter group of organisms one might call *biochemic pathogens*.

Would it not be possible for the biochemically-minded bacteriologists or the bacteriologically-minded biochemists to give us a symposium or a collective view of the facts as they are known to the experts, making, at the same time, a definite attempt to relate them to the problem of nutrition?

- R. HUGHES, M.B., F.R.C.S.,  
Senior Medical Officer.

KHASI HILLS WELSH  
MISSION HOSPITAL,  
SHILLONG,  
1st July, 1944.

## Service Notes

### APPOINTMENTS AND TRANSFERS

THE VICEROY AND GOVERNOR-GENERAL has been pleased to make the following appointments on His Excellency's personal staff:—

#### To be Honorary Surgeons

Colonel V. N. Agate, *vice* Colonel (Actg. Brigadier) W. Ross Stewart, C.I.E., vacated. Dated 20th October, 1943.

Colonel A. H. Harty, C.I.E., *vice* Colonel (Local Brigadier) G. Covell, C.I.E., V.H.S., vacated. Dated 8th November, 1943.

Lieutenant-Colonel G. H. Mahony, I.M.S. (Retd.), is temporarily re-appointed as Civil Surgeon, Darjeeling, for the period from the 3rd February, 1944, to the date of his making over charge to Major E. G. Montgomery.

Lieutenant-Colonel P. A. Dargan, I.M.S. (Retd.), was appointed Civil Surgeon, New Delhi, with effect from the afternoon of the 13th April, 1944.

Lieutenant-Colonel F. H. Whyte is appointed Civil Surgeon, Simla West, with effect from the forenoon of the 17th April, 1944.

Lieutenant-Colonel M. Das, M.C., took over executive and medical charge of the Alipore Central Jail from Mr. H. W. Shea and Dr. B. B. Roy respectively in the forenoon of the 6th June, 1944.

Major E. G. Montgomery, Inspector of Civil Hospitals, is appointed as Civil Surgeon, Darjeeling, with effect from the date on which he relieves Lieutenant-Colonel G. H. Mahony, I.M.S. (retired).

Major John Brebner made over charge of the Chittagong Jail to Major P. L. O'Neill, in the forenoon of the 6th May, 1944.

Captain W. A. Browne, on reversion from military duty, is appointed as Civil Surgeon, Rajshahi.



## INDIAN LAND FORCES

SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commissions)

## To be Captains

- Ainuddin Ahmed. Dated 23rd December, 1941.  
 Joginder Singh Puri. Dated 15th March, 1944.  
 Kartik Chandra Ganguly. Dated 23rd March, 1944.  
 Kanaparti Srinivas. Dated 12th April, 1944.  
 Sri Krishna Sen. Dated 19th April, 1944.  
 (Miss) Simantini Balkrishna Kekre. Dated 7th February, 1944.  
 (Miss) Louise Mary Tellis. Dated 16th February, 1944.  
 (Miss) Teresa Dominic. Dated 22nd April, 1944.  
 Doodipala Narsimha Reddy. Dated 14th March, 1944.  
 Ankes Kumar Chakrabarti. Dated 14th February, 1944.  
 (Miss) Florence Annie Griffiths. Dated 24th May, 1943.  
 Babu Ram Sharma. Dated 20th November, 1943.  
 Mohamed Vajhee-ud-Din. Dated 20th April, 1944.

SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commission)

## (WITHIN INDIAN LIMITS)

## To be Captain

- Sailendra Prosad Mitra. Dated 8th June, 1943.

## INDIAN LAND FORCES

FOR SERVICE WITH THE ROYAL INDIAN NAVY  
(Emergency Commissions)

## To be Captain

- Vijay Gaurishanker Daftary. Dated 2nd December, 1943.

## To be Lieutenants

- Avadhut Vishnu Bal. Dated 14th January, 1944.  
 M. P. Deshmukh. Dated 14th April, 1944.

## INDIAN LAND FORCES

FOR SERVICE WITH THE INDIAN AIR FORCE  
(Emergency Commission)

## To be Captain

- Gour Gopal Chatterjee. Dated 5th November, 1943.

## PROMOTIONS

The undermentioned officer is granted the honorary rank of Colonel on reversion to pension establishment :—

- Brevet-Colonel A. M. Dick, C.B.E. (Retd.). Dated 13th May, 1944.

The undermentioned Indian Medical Service Officer is advanced to the list of special selected Lieutenant-Colonels :—

- Lieutenant-Colonel H. E. Murray. Dated 18th May, 1944.

## INDIAN LAND FORCES

SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commissions)

## Lieutenants to be Captains

- K. B. Krishnaswami Rao. Dated 2nd May, 1944.  
 P. M. Xavier. Dated 3rd May, 1944.  
 L. G. R. Hull. Dated 4th May, 1944.  
 G. Natarajan. Dated 5th May, 1944.  
 D. F. O'Malley. Dated 7th May, 1944.  
 M. Thomas. Dated 8th May, 1944.  
 A. R. Chowdhury. Dated 11th May, 1944.

12th May, 1944

- A. Bhattacharya. H. K. Dutt.

14th May, 1944

- G. C. Dey. J. K. Adak.  
 J. C. A. Dique.

15th May, 1944

- R. D'Souza. J. F. Bonjour.  
 T. S. Rao. Dated 17th May, 1944.

20th May, 1944

- S. Subramaniam. K. Parthasarathy.  
 K. M. Rao.

- B. R. Sharma. Dated 7th January, 1944.  
 M. A. Chowdhury. Dated 16th May, 1944.  
 B. Sen Gupta. Dated 21st May, 1944.  
 D. J. W. D'Costa. Dated 22nd May, 1944.  
 C. J. D'Netto. Dated 30th May, 1944.  
 (Miss) F. A. Griffiths. Dated 14th August, 1943.

## (WOMEN'S BRANCH)

## Lieutenant to be Captain

- Miss N. M. Bail. Dated 27th May, 1944.

## INDIAN LAND FORCES

FOR SERVICE WITH THE ROYAL INDIAN NAVY  
(Emergency Commission)

## Lieutenant to be Captain

- M. P. Deshmukh. Dated 29th May, 1944.

## RETIREMENTS

- Lieutenant-Colonel H. A. Khin. Dated 11th May, 1944.  
 Lieutenant-Colonel E. W. O'G. Kirwan, C.I.E. Dated 18th May, 1944.

## Publishers' Notice

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The Editors of *The Indian Medical Gazette* cannot advise correspondents with regard to prescriptions, diagnosis, etc., nor can they recommend individual practitioners by name, as any such action would constitute a breach of professional etiquette.

## Original Articles

### SOMATIC TÆNIASIS

(*SOLIUM CYSTICERCOSIS*)

By GEORGE R. McROBERT, C.I.E., M.D., F.R.C.P.

LIEUTENANT-COLONEL, I.M.S.

Professor of Medicine, Madras Medical College, and  
Physician, General Hospital, Madras

It is now well known that infestation of the muscles, eyes and brain with the cysticerci of a cestode occurs in India. MacArthur (1934) and other officers of the R.A.M.C. have drawn attention to cysticercosis as a cause of epilepsy in soldiers who have served in India. The mode of infection is doubtful, as only a small proportion of such epileptics admit infection with a tapeworm.

Diagnosis of somatic tæniasis is usually made on x-ray evidence—the partially calcified cysticerci showing up well on skiagrams.

The case now reported was referred to me for investigation in August 1941 by Lieut.-Col. A. Innes Cox, I.M.S., then District Medical Officer, Madura. Lieut.-Col. Cox had confirmed his diagnosis of somatic tæniasis by biopsy—the material being reported as cysticercus by the Professor of Pathology, Madras Medical College.

The patient was a cultivator from a village in the Ramnad district. He was 25 years of age, and had always been of a slim build. He went to hospital because of a gross alteration in his physical appearance which had come to resemble that of a professional wrestler—to the amusement of his friends and dismay of his household (figure 1, plate XIX). He had noted a change over a period of six months only.

The patient had never kept pigs at any time, and was not in the habit of eating pork. He had eaten no pork within the past four years prior to admission, and was not aware of having harboured a tapeworm at any time.

His appearance was certainly suggestive of a professional strong man. Palpation of the neck, shoulders and thighs revealed the presence of thousands of slippery, blubbery swellings. The superficial ones slid under the fingers like soft peas, but the palpating hand got the impression of great masses of such material throughout the whole of the pectoral and pelvic girdles, upper arm muscles, thighs and hips. Multitudes of swellings could be seen in the cervical and facial regions, visible from a distance (figure 2, plate XIX) when the masseter muscles were clenched.

The patient was radiographed from head to foot on several occasions, with rays of different intensities and with various filters, and at no time during his four and a half months' stay in hospital was there the slightest x-ray evidence of the presence of anything abnormal in the tissues.

Blood examination revealed no abnormality (eosinophils 6 per cent). The Wassermann and Kahn reactions were negative.

No ova were present in the faeces. Exhaustive examination of the central nervous system revealed no abnormality. Ophthalmoscopic appearances were normal.

In order to obtain further information, I requested my colleague, Major F. M. Collins, F.R.C.S., to remove a number of cysts from the neck.

Immediately after the operation, six cysticerci were swallowed with a little fruit jelly on an empty stomach by a volunteer who was free from any intestinal worm infection and who was willing to be kept under daily observation. In twelve months, with frequent examination of the stools, I failed to find any evidence of infection.

A number of cysts were sent to Dr. Maplestone of the School of Tropical Medicine, Calcutta, and he kindly reported as follows:

'I have no hesitation in identifying the cyst as *C. cellulosæ*. The hooks numbered 24 and were typical in size and shape according to my own records, from a large number of cysts taken from pigs.

The hooks were as follows:—

Short hooks	..	..	114-126 $\mu$
Long hooks	..	..	159-163 $\mu$

well within the normal limits of my standard figures.

The measurements are a good deal lower than are usually given in books, but I am satisfied that this is a characteristic of *C. cellulosæ* of Indian origin.

My standard figures are:—

Number of hooks	..	..	22-28
Short hooks	..	..	90-130 $\mu$
Long hooks	..	..	133-169 $\mu$

The patient was himself most anxious for something to be done. It was fully recognized that serious symptoms do not as a rule appear until the cysts become moribund and swell up. Most reported cases, however, have been in a late stage with calcification demonstrable by x-rays. It was thought worth while to try some treatment whilst the cysts were still young. Deep x-rays were out of the question on account of the generalized nature of the infection.

On the 3rd September, 1941, a small tentative dose of 1.5 c.cm. of fantorin (G. L.), an organic antimony compound (in the use of which we have wide experience in this hospital), was administered intramuscularly. Two hours later, in the midst of an animated conversation with a neighbour in the ward, the patient got a violent epileptiform convulsion with loss of consciousness which lasted 9½ hours.

In the first hour there were four attacks of generalized convulsions each lasting about one minute, with no localizing signs.

Lumbar puncture revealed fluid under normal pressure with no abnormality in cellular constituents or chemical content.

Three hours later there was a generalized convulsion lasting a few seconds only. During the period of unconsciousness, the knee and ankle jerks were abnormally brisk, and bilateral extensor plantar responses were elicited.

It was thought probable that the fits and period of unconsciousness were due to the action of the fantorin on the cysts and not to specific sensibility to organic antimony, as we have had no experience of such fits after the use of much higher doses of fantorin in other diseases.

It was decided after a period to try the effect of antimony again—first as sodium antimony tartrate in small and increasing doses, and as fantorin again. Sodium antimony tartrate was given intravenously in doses of  $\frac{1}{2}$  grain, 1 grain,  $1\frac{1}{2}$  grains and 2 grains (in 2 per cent solution) at 2-day intervals without producing cerebral irritation. Fantorin injections were then begun again commencing with  $\frac{1}{2}$  c.cm. intramuscularly followed by 1 c.cm. and  $1\frac{1}{2}$  c.cm. (the initial dose). With  $1\frac{1}{2}$  c.cm. the patient felt a little giddy and lay quiet for half an hour. Three days later  $1\frac{1}{2}$  c.cm. was again given without any untoward effect and then at 3-day intervals 2 c.cm. and 5 c.cm. were injected on seven occasions. In all 48 c.cm. of fantorin were administered over a period of just over two months without serious symptoms except on the first occasion of administration.

Six weeks after his last injection, the patient demanded to be discharged as he was feeling better and wanted to return to his village.

One gained a clinical impression of improvement, but it would not be safe to say more, and at the time of his discharge there was still no x-ray evidence of cysticercosis.

Since the day of his discharge, I have endeavoured to get into touch with the patient through various channels, official and otherwise, but have failed to do so, as often happens in attempted follow-ups in this country.

### Summary

A case is reported in which there was hyperinfestation of the tissues with cysticerci of *T. solium*. X-ray evidence was negative.

Alteration in the bodily configuration was obvious to all, and caused the patient to seek advice.

Fits developed when a small dose of organic antimony was injected.

A feeding experiment with newly excised cysts failed to produce transmission to another human being.

Cyst measurements are given.

The mode of infection remains a mystery but in a communication to me in August 1941, Dr. Maplestone suggested the possibility of infection with *T. solium* with rapid digestion of the worm going on all the time, so that segments are never passed, and the patient is unaware of the infection. When the head dies, naturally it may be passed without the patient being aware of it.

In this case repeated doses of male fern and microscopic examination of the stool negatived the presence of the worm at the time of admission into hospital.

I wish to express appreciation of the help given by Dr. P. Maplestone in verifying the identification of the cysts and in supplying measurements and comments on the possible mode of infection.

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## A NEW METHOD OF ARTIFICIAL RESPIRATION

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THE two main recognized methods of artificial respiration, namely, Schafer's and Silvester's, depend for their efficacy on the elastic recoil of the chest wall and diaphragm, which can happen only when the integrity and tonicity of the muscles of the respiration are maintained. Schafer's (1907-8) method consists in 'laying the subject prone, and pressing gradually for three seconds with both hands close together flat on the back over the loins, the fingers extending over the ribs. The abdominal contents are indirectly pressed upon, driving the diaphragm up into the chest and forcing air out of the lungs thereby'. When the pressure is released, the diaphragm is expected to move down by its own elasticity, and perform the inspiratory process in consequence. Silvester's method consists in squeezing the chest with the arms and elbows of the patient. The elastic recoil of the chest wall is supposed to help the inspiration of air.

Both methods are useful but very imperfect. The weak points in Schafer's method have been clearly described by Evc (1943). In the deeply unconscious state, whether due to drowning, electrocution or general anaesthesia, the elastic tone of the respiratory muscles fails progressively. Barclay has shown by radiograph that in the prone position the diaphragm is pushed up into the full expiratory position. This will be accentuated in a toneless body. Silvester's method, which depends on the elastic recoil of the chest wall, also fails in the semi-final stages of incomplete death when the intercostal muscles would have lost their tone. The incompleteness of both the methods is due to their efforts being directed towards helping the expiratory process rather than the process of inspiration. When the tone of the respiratory muscles is partially or completely lost, the thorax will necessarily be in the position of partial expiration. Hence a simple method which would actively help to bring the chest to a position of inspiration will be more efficient than the other methods which help only the expiratory process by trying to place the chest in the exaggerated expiratory position. One should aim at expanding the lung rather than squeezing the already contracted lung.

*Mechanism of respiration.*—Quiet normal breathing is mainly diaphragmatic. Contraction

of the diaphragm causes expansion of the lung in the vertical axis by bringing the dome to a lower level. The action of the diaphragm lies also in raising the lower ribs. In thoracic breathing, the capacity of the chest is greatly increased by the ribs being raised and thereby being made to assume a more horizontal position. There is also widening of the lower costal margins. In forced inspiration, the expansion of the lung is mainly due to the change of shape of the chest brought about by the upward movement of the anterior portions of the ribs. Hence inspiration will be easily brought about by any method which brings the chest wall to the high inspiratory position and shape.

*The method (see figures 1 and 2, plate XX).*

Experimenting on warm cadavers and on patients under deep general anaesthesia, I found that by pulling on the lower costal margins in an upward and outward direction with the hooked fingers of both hands, the chest can be made to assume the raised position of inspiration. Release of the pull coupled with gentle pressure on the lower ribs with the palms of the hands is quite sufficient to bring about the expiratory process.

If the patient is on a cot or on an operation table, lying on the back, the operator stands at the head end and places the palms of the hands on the lower part of the chest the middle fingers being on the anterior axillary lines. The fingers are hooked round the lower costal margins on both sides. The pull is made in an upward and outward direction, thereby raising the anterior portions of the ribs as well as widening the lower costal arches. After a steady pull of three seconds, the pull is released and the chest is gently pressed upon in a downward and inward direction, while the extended fingers exercise the same pressure on the abdomen. Doing this about 12 or 15 times a minute brings about a respiratory exchange of over 7,000 c.cm. of air. The expansion of the chest and outward stretching of the diaphragm due to widening of the lower costal arches also help the venous return of the blood.

With the patient in the face-down position, the operator assumes the same position as before, but his hands are brought underneath the chest and the lower costal arches are pulled upwards and outwards.

I had the opportunity to give an extensive trial to this method on a case of unconsciousness due to hæmorrhage in the brain. On admission the patient was deeply comatose and had Cheyne-Stokes' breathing. His pulse was slow. In half an hour the breathing stopped. The pulse also could not be felt. I tried the above method of artificial respiration, never expecting to bring back his pulse. I found to my surprise that after 3 or 4 attempts the pulse at the wrist returned. As respiration was not restored, artificial respiration was continued. For purposes of comparison, one of the surgeons tried the Silvester's method. It was found to be much less effective, as the

respiratory muscles were toneless. The patient was kept alive for six hours, including the period of operation lasting for over an hour, by this method of artificial respiration alone until he was put in the 'iron lung'. I observed also that whenever artificial respiration was stopped for a few seconds his pulse began to rapidly fail, showing that this method helps in restoring the circulation as well. The surgeons and the anaesthetists of the hospital were quite satisfied with the efficacy of the method.

Cordier (1943) lays down three requirements for judging the efficacy and efficiency of any particular method of artificial respiration. The method must (1) give sufficient pulmonary ventilation of a normal subject at rest, (2) stimulate the heart and circulation to help respiratory exchange and transport of oxygen to the tissues and (3) be harmless in themselves, easy of execution and rapid in attaining results.

In order to satisfy the first criterion I experimented on a patient under moderately deep anaesthesia with the help of Captain F. M. F. Forrest, the anaesthetist, and Captain A. K. Bose. The muscles were relaxed and he was in a state of comparative apnoea. The amount of air expelled by pressure on the lower ribs after the inspiratory pull on the costal margins was collected in the rebreathing bag of a Boyle's apparatus and measured. This was compared with the amount collected by Schafer's and by Silvester's methods. The results were as follows :—

Schafer's method	..	255 c.cm. average
Silvester's method	..	425 c.cm. „
New method	..	836 c.cm. „

The marked difference in the ventilation is evidently due to the new method assisting both the inspiratory as well as the expiratory processes.

I am of opinion that this method satisfies also the second requirement laid down by Cordier. In the case reported above, the pulse returned to the wrist after 3 or 4 attempts at artificial respiration. During the process of aided inspiration, the tips of the hooked fingers of the left hand of the operator exert some pressure on the left side of the diaphragm and thereby probably stimulate the heart mechanically. As the chest expansion is artificially done, the venous return is aided by increased negative pressure inside the chest during the process of inspiration.

The method is absolutely harmless and easy to execute. For cases of suspended respiration, particularly during anaesthesia, this method comes in very handy indeed, as it causes the least disturbance to the patient. In the case of intracranial hæmorrhage reported above, where-in artificial respiration was successfully carried on throughout the period of operation as well, Schafer's and Silvester's methods were not feasible.

The advantages of this method therefore are :—

(1) Better ventilation due to active inspiration as opposed to active expiration in the other methods.

(2) Helping the venous return.

(3) Less strain and bodily exertion on the part of the operator.

Eve's rocking method has its own uses, but on the operation table particularly, the new method is most efficient and most handy.

My grateful thanks are due to the surgeons and anaesthetists of a general hospital for allowing me to give an extensive trial of this new method on their cases. I am grateful to my Commanding Officer for kindly allowing me to experiment on an anaesthetized patient and to Captains F. M. F. Forrest and A. K. Bose for their assistance.

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### BILATERAL PRIMARY CARCINOMA OF THE FALLOPIAN TUBES

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PRIMARY carcinoma of the tubes is extremely rare, and its bilateral occurrence is necessarily all the more rare. The condition was first described by Raynaud in 1847, and the first pathological description was given by Rokitsansky in 1861. Doran reviewed one hundred cases up to the end of 1910. Bower and Clark in 1925 added another series of one hundred and thirty-three cases collected from various sources. In 1929 Wharton and Krock brought the subject up to date with a collection of two hundred and forty-four cases. Kahn and Norris (1934) in their excellent review brought the literature further up to date, collecting two hundred and seventy reported cases and adding four more of their own. In all, up to the end of 1935 three hundred and forty-nine cases of tubal carcinoma had been recorded. Since then McGlinn and Harer (1933), Martzloff (1940), Phaneuf (1938), Smith (1932), Dannreuther (1935), Robinson (1936), Tuta and Stuhr (1941) and others have each added one or two further cases. Most of these reports have been from the United States of America. A report of this condition is perhaps the first of this kind from India.

Considering the frequency of malignant growths in other pelvic organs, it is difficult to explain why they are so rare in the tubes. Vest (1914) reported only four cases in 19,000

gynaecological admissions from the John Hopkins Hospital; Barrows (1927) three cases in 30,000 such admissions at the Bellevue Hospital, New York; Holland (1930) reported nine cases in 10,000 salpingectomies done at the Mayo Clinic; and from the Cleveland University hospitals only two cases are reported among 22,300 gynaecological admissions. The incidence of these new growths, therefore, according to Robinson, ranges between 0.03 and 0.31 per cent of the gynaecological affections.

Tubal tumours are well classified by Watkins (1933) into those arising from epithelial cells, from connective tissue cells, or from embryonal cell rests. The primary tumours originating from epithelial tissue include carcinoma, endometrioma, adenoma, papilloma, endothelioma, cyst and chorion epithelioma. Among these, carcinoma is the commonest.

Tubal carcinoma is seen equally in parous and nonparous women. Age does not seem to be significant. The majority seem to occur between forty and sixty, even though the youngest case reported was eighteen and the oldest eighty.

There is a general impression among gynaecologists that pelvic inflammation is a predisposing factor, and the evidence in favour of this view is the high incidence of closed fimbriae and the comparatively high rate of sterility. There appears however to be no real connection between carcinoma and salpingitis. Kelly (1928) believes that the new growths of the tubes arise from the mucosa of the aberrant endometrial transplants.

Three types of carcinoma of the fallopian tube have been described: the papillary, the adenomatous and the alveolar. Many pathologists believe that these are merely morphologic variations in the development of the disease, the papillary formation being the earliest, the adenomatous and the alveolar being the later stages of the papillary, produced by confluence of the papillary folds. It is not uncommon to see all the stages in the same specimen. The papillary carcinomas may frequently develop from a benign papilloma, or arise independently from the tubal mucosa. They occur most frequently in the distal half of the tube. The distended tube presents an appearance similar to that of a hydrosalpinx, but it is much firmer to the feel. Fully grown tumours, when seen late, generally show a certain amount of cystic change due to associated necrosis and hæmorrhages within the tumour.

Grossly, carcinoma of the tube is difficult to differentiate from a benign papilloma, particularly when there are no growth metastases. The benign tumour most often projects out of the fimbriated end as a cauliflower-like mass, and shows no local invasiveness. Microscopically the lining cells appear single-layered, and are of uniform size. The nuclei manifest only occasionally mitotic figures, and the nucleoli are not prominent.



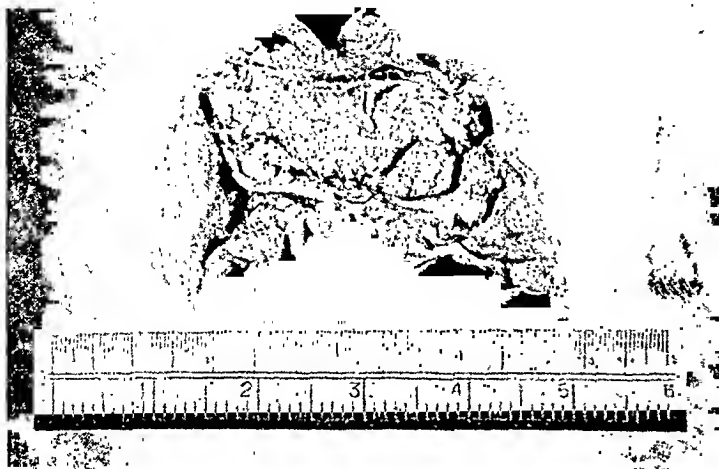


Fig. 1.—Left fallopian tube.

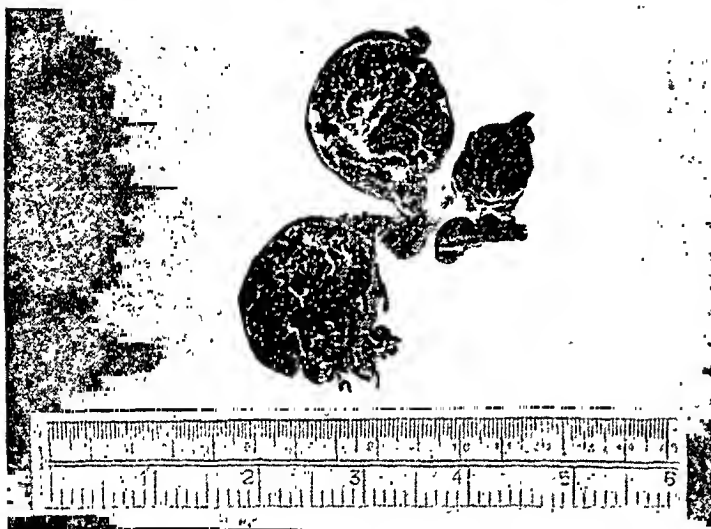


Fig. 2.—Right fallopian tube.

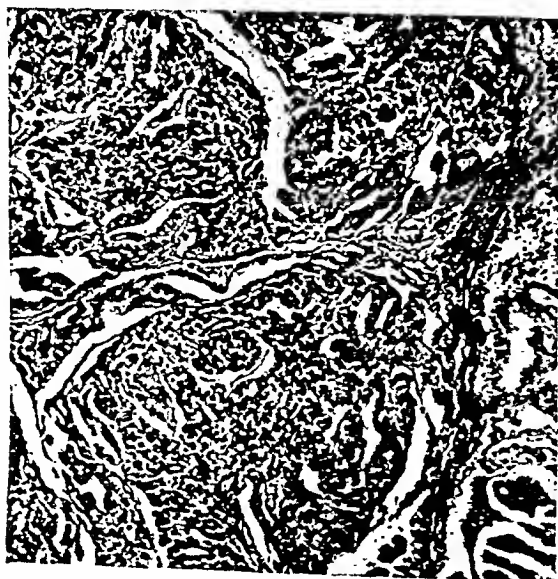


Fig. 3.—Photomicrograph (X 100). (Note the papilliferous, the alveolar and the adenomatous variations.)

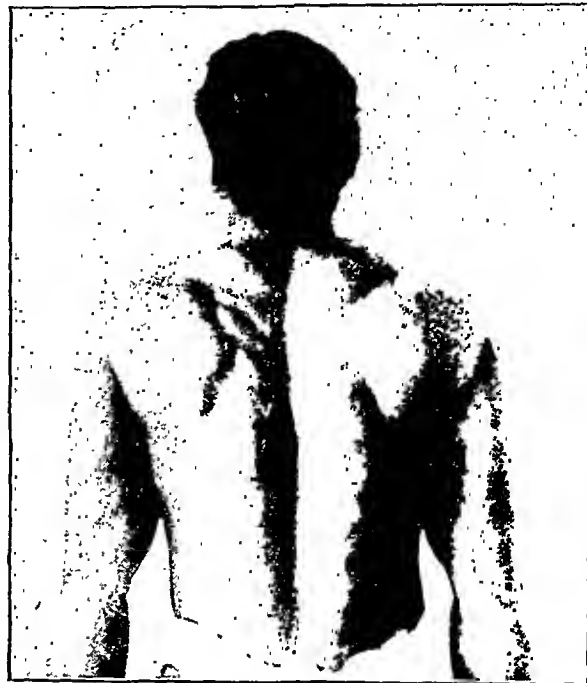


Fig. 1.



Fig. 2.





Fig. 1.—An advanced case which failed to respond to treatment.



Fig. 2.—Before treatment.



Fig. 3.—After treatment.

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Fig. 1.—Process of inspiration.



Fig. 2.—Process of expiration.

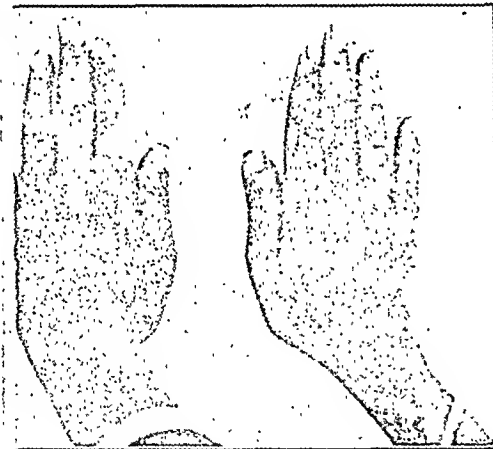


Fig. 4.—The characteristic blackness of the knuckles. It is not a rash as in pellagra.

Malignant growths usually measure between 1 and 15 cm. in diameter, the size depending somewhat upon the duration. Most often the mass has invaded the tube and the neighbouring structures before the surgeon recognizes the disease. Clinical and pathologic experience has demonstrated that in one-third of the cases, metastasis is seen in distant locations even before the tubal wall has become involved. The spread is by lymphatics and not so much by contiguity. Peritoneum, ovary or fundus uteri may be involved through metastases or by direct extension. Microscopically the tumour cells appear several layers deep, irregular in size, and shape, with large nucleoli. The nuclei are deeply stained. The cells are generally vacuolated. The sub-mucosa is involved and shows foci of round cell infiltration.

Clinically there is no pathognomonic symptomatology in primary carcinoma of the tubes. The individuals may complain of irregularity of menstrual flow with some increase in frequency. Generally they complain of slight bloody watery discharge which often occurs in gushes. Pain in the lower abdomen is quite early, and is probably due to stretching of the tubal musculature. The presence of one or all the symptoms above mentioned, a soft unilateral or bilateral mass, with a normal cervix, uterus and ovaries, should remind one of this rare gynaecological condition. The difficulty arises during vaginal examination to exclude commoner tumours of the adnexa.

The treatment is pan-hysterectomy with removal of both ovaries and tubes. Post-operative deep x-ray or radium therapy is indicated in every case. Unfortunately in most of the cases reported, either adhesions or glandular involvement have already taken place, and the prognosis has been consequently very poor.

#### *Report of a case*

*Case.*—Patient J., aged 45, was admitted under the care of one of us (G. A. G.) complaining of red and offensive vaginal discharge for one year. She has no children and in fact had never conceived. She had a normal menopause three years previously. Menstrual periods were normal at first, but later they became profuse, and for four to five months before the menopause very profuse.

On examination, a large irregular mass was felt in the lower abdomen, mainly on the left side but extending into both the iliac fossae. On the left it reached almost to the umbilicus, and was hard and partly fixed. On vaginal examination there was no discharge. A large tumour was palpable, irregular, tense, hard and fixed to the uterus. The pre-operative diagnosis was multiple fibro-adenomata.

*Operation.* The patient was operated on on 17th August, 1943, by one of us (G. A. G.).

A large cystic tumour was found on the left side, completely bound down in the pelvis. The transverse colon was adherent to the mass anteriorly over an area of two inches circumference. The cyst was inflamed and reached almost to the level of the umbilicus. During an attempt to dissect out the cystic mass, the cyst ruptured, exuding dark serous blood-stained fluid. A papillomatous mass was clearly seen within the cyst, and small pieces broke off along with the exudate. A small piece of the cyst wall was so firmly adherent to the transverse colon that it could not be removed.

A smaller tumour presented itself on the other side. This was however solid and not inflamed. There were just a few fine adhesions fixing the tumour to the pelvis. It was found to be a tumour in connection with the right tube, and from the abdominal ostium a piece of papillomatous growth was extruding. The right tube was removed along with the ovary. The left ovary was not seen.

The uterus was small and there was a small subserous fibroid on the posterior wall. The uterus was not removed as it was considered that the condition of the patient did not warrant further operation.

The liver was normal to palpation and no glands were enlarged. The Kahn test was negative.

The patient ran a temperature between 100°F. to 101°F. for ten days, and then recovered.

#### *Pathological report (V. R. N.)*

The left tubal mass (figure 1, plate XIX) is roughly heart-shaped, weighs 63 gm. and measures 7×6×4½ cm. The base of the tumour is on the isthmic end of the tube. The tubal mass is partly covered with a pad of fat, which is probably the adherent mesentery. The posterior surface is congested. There is an irregular opening in that region, through which pieces of tumour mass are exuding along with darkish fluid. On opening, the tumour wall is thick and hyalinized. There is no evidence of any mucosa. Dilated capillaries are seen on the external surface. The tumour is a cauliflower-like mass, pinkish-grey in colour and very friable. On the surface of the irregularly globular mass arise a few papular excrescences which are loosely held, varying from ¼ to 1 cm. in diameter. Thick strands of connective tissue support this friable mass. There is no evidence of any calcification, though the connective tissue gives a gritty feeling on cutting.

The right tube (figure 2, plate XIX) is a retort-shaped mass, the neck of the retort being towards the isthmus. It weighs 25 gm. and the diameter at its widest is 4 cm. The right ovary is shrunken and is situated at the inferior border of the neck. The tumour mass is mostly situated at the distal third of the tube. The fimbriae are involved in the tumour process, and appear like a worn-out shaving brush with short bristles. The tumour is greyish-white in colour. Small dilated veins are seen traversing over the external surface of the tumour. On cutting, the tumour wall appears to be thinned out, translucent, and parchment-like; it possibly contains the remains of both the serosa and muscularis. The tumour mass is friable and fills tightly the distended cavity of the tube. Occasional haemorrhages are seen scattered through the tumour.

*Microscopical* (figure 3, plate XIX). The background appears to be formed of loose connective tissue strands supporting the tumour cells. At the tubal wall, the tumour connective tissue is much denser and contains a large number of capillaries and lymphatics. There is diffuse round-cell infiltration. The arrangement of the tumour cells is in some places distinctly papilliform, while in other places it is alveolar. The cells are polyhedral with dark staining nuclei and one or two large nucleoli. The outline of the cells is not distinct and the cytoplasm is highly vacuolated. Mitotic figures are present in considerable number. In several places the compactly arranged papilliferous folds present an appearance of alveolar formation. Areas of necrosis with homogeneous staining are not uncommon. The tubal wall consists of layers of compact partly-hyalinized connective tissue and thinned out muscularis. The tubal wall is infiltrated with small round cells and occasional eosinophilic cells. The blood capillaries are dilated and filled with blood. The lymphatics are distended. Tumour cells are not seen in the lymphatics. Microscopic appearance is similar to that on the left.

#### *Summary*

Primary bilateral carcinomas of the fallopian tubes are exceedingly rare. About three

hundred and seventy-five cases have previously been recorded. Two possible predisposing factors in the aetiology of the carcinoma are the presence of benign papilloma and of pre-existing inflammation, but there is no strong evidence to incriminate either. The three microscopic varieties of cancer described are really different stages of a similar growth.

The malignant growths differ from the benign papilloma in their cytology. One-third of them show metastasis even before the tubal wall is involved. The spread is by lymphatics to the regional lymph nodes, peritoneum and fundus of the uterus.

There is no single symptom diagnostic of the disease. Generally the individual is past the menopause and complains of a reddish vaginal discharge and lower abdominal pain. Vaginal examination reveals a mass in connection with the adnexa. Besides the common tumours of the region, carcinoma of the fallopian tube may be the cause.

Our thanks are due to Dr. K. C. Pani, Krishnarajendra Hospital, Mysore, for the photographs and micro-photographs.

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#### PARA-SPRUE

##### A STUDY OF 22 CASES

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A CONDITION of chronic diarrhoea associated with anæmia and sore mouth, suggestive of sprue, has long been known in this country, and it is

usually regarded as a chronic deficiency state. Nicholls (1918) and Elders (1919) put forward vitamin deficiency as its cause, while McCarrison (1919) produced a sprue-like condition in monkeys fed on a vitamin-free diet. Acton and Knowles (1928) found a similar condition developing after Flexner bacillus infection, which they attributed to secondary invasion of ulcers in the intestine with streptococci, passing into what they called 'pre-sprue' condition. Napier (1939) observed a frequent association of nutritional macrocytic anæmia with diarrhoea and dysentery, and it was found fairly common amongst pregnant women especially of the poorer class (Napier and Neal Edwards, 1941). The patients complain of indigestion, flatulence, anorexia and asthenia, and these symptoms together with loose, irregular motions passed at any time of the day, glossitis, macrocytic anæmia and emaciation constitute a distinct clinical syndrome. For this condition the word 'para-sprue' has been used in this institution for the past few years. The purpose of this paper is to report the findings of a series of consecutive cases treated by us during a period of about 3 years.

#### The patients

The subjects of this analysis were 22 patients, admitted to the hospital attached to this school, in whom a diagnosis of para-sprue was made. The series included 6 Europeans, 4 Anglo-Indians and 12 Indians (Bengali 7, Behari 3, United Provinces 1 and Assamese 1). There were 16 males and 6 females. Their age distribution was as follows:—

Under 30 years ..	..	..	2
30 to 40 ..	..	..	10
41 to 50 ..	..	..	5
51 to 60 ..	..	..	5
			22

*History.*—From the history of the duration of illness the patients can be divided as follows:—

Duration	Number of cases
6 to 8 months ..	.. 7
1 to 2 years ..	.. 13
Above 2 years ..	.. 2

The average duration of the disease on admission was about one year. There was a history of previous attacks of dysentery or colitis in 14 cases, which were in many instances not properly treated, and in most of them this was the beginning of the illness. A chronic diarrhoea followed, but there were alternating periods of diarrhoea and constipation in 4 cases. Invariably there was restriction of diet, either voluntarily or under medical advice. One patient stated that she was practically on barley water for about 2 months before admission to the hospital. There was no other case in the family of any of these patients.

*Clinical features.*—The onset was insidious. Diarrhoea was a common feature, the daily

number of stools varying from 2 to 4 in 10 cases, 5 to 10 in 10 cases and more than 10 (up to 15) in 2 cases. The faecal character was as follows :—

Character	Number of cases	REMARKS
Watery diarrhoea ..	8	Pale colour in two.
Dysenteric motions—		
(a) with mucus ..	6	Frothy in one.
(b) with mucus and occasional blood.	2	..
Bulky stools ..	6	Pale and frothy in two.

All except one had sore tongue; the observations on this point on admission are shown below :—

Red patches ..	9 cases	
Red and glazed ..	5 "	
Sore and fissured ..	2 "	(1 with pigmented patches).
Flat and smooth ..	2 "	
Glossitis and stomatitis ..	2 "	
Red tip and margin ..	1 case	

Other symptoms included loss of weight in all, flatulence in 11, anorexia in 9, low fever in 4 and nausea in 2 cases. Twelve patients were emaciated, and 6 had œdema of the legs. The abdomen was soft, flabby and distended in most cases, but sunken in a few. The right iliac fossa was tender in 4, and the colon was palpably thickened in 6 cases. Flatulent distension and gurgling was common but variable. Some patients felt much discomfort as they were 'unable to pass wind'.

#### Laboratory investigations

A full blood count was done on admission and repeated usually at weekly intervals, the initial counts being shown in the table. Four patients were markedly anæmic (hæmoglobin of 6.6 grammes or less), 7 were moderately anæmic (over 6.6 grammes up to 9.6 grammes) and 8 were slightly anæmic (over 9.6 grammes). The anæmia was macrocytic and hyperchromic. Leucopenia was present in about one-third of the cases. The van den Bergh reaction was usually negative, and there was as a rule no reticulocytosis (except after liver therapy). The sedimentation rate was variable, being 20 mm. or less in 9 out of 20 cases. The Wassermann test was done in 21, with negative results. The gastric acid curve was normal in 13, one had hyperchlorhydria, while 8 had achlorhydria (with response to histamine in 5, and without response in 3). The faecal fat was analysed\* after keeping each patient on a standard diet containing not more than 100 gm. of fat, for 3 consecutive days. In this series the total fat was 20 to 25 per cent of the weight of dried faeces in 9 cases, 26 to 30 per cent in 7 cases, 31 to 33 per cent in 5 cases, and 42 per cent in one case only. It was adequately split in most cases. The glucose tolerance test

(after 50 gm. of glucose by mouth) was done in 15 cases. The fasting blood sugar level varied from 82 to 110 mg. per 100 c.cm. In 2 cases there was no rise of blood sugar within 3 hours, in one there was a slight rise (10 mg.) in the third hour specimen, and in 5 the maximum rise was less than 30 mg., producing a definitely low curve. In the remaining 7 cases the glucose curve was practically normal. The intravenous glucose tolerance test was done in 6 out of 8 patients with a flat or low curve. There was an immediate rise of blood sugar (maximum 222 mg. per 100 c.cm.) in all of them, coming down to normal level within one hour. These results indicate that in about half of these cases glucose absorption was poor, but the power to utilize it from blood was unaffected. The stools were repeatedly examined for ova, protozoa and bacteria, all with negative results except in 2 in which *Bacterium flexneri* was isolated. X-ray examinations of the intestine after a barium meal were done in 2 cases, but the results were inconclusive, and it was not possible to continue this investigation in other cases owing to scarcity of films.

#### Treatment

This consisted of hospital rest and management, treatment for diarrhoea, anæmia and achlorhydria, and giving a diet as liberal as possible according to the patient's condition, starting more or less in the proportions of sprue diet (high protein, low fat and low carbohydrate), but not following its strict dietary regime. The patients with much diarrhoea and anorexia had a liquid diet in the beginning (often supplemented by intravenous glucose) but solids were added quickly, and the latter seemed to agree better than liquids. Full hospital diet including meat, perhaps with some modification avoiding curries, etc., was allowed as soon as possible.

Six patients were given no medicine to control the diarrhoea; their stools were formed soon after the diet was changed from the low caloric fluid diet that they were having at home to a well-balanced diet along with parenteral administration of liver extract. Nine were given a sodium sulphate mixture, a drachm per dose, or castor oil emulsion 3 or 4 times a day for about 3 days, followed if necessary by bismuth or kaolin, while 5 had sulphaguanidine in the usual doses according to weight of the patient. The last named remedy appeared most efficacious in stopping diarrhoea. Recurrences of diarrhoea occurred in a few patients while undergoing treatment in the hospital but usually subsided in a short time with or without any treatment.

Liver was given by injection to all cases, the preparation used being crude extract such as Lilly's, T.C.F. (whole), etc., which were repeated as deemed necessary. Liver soup was also prescribed, but some Indian patients did not like it and ultimately refused it. Administration of

\* The estimations of faecal fat and blood sugar were done in Dr. J. P. Bose's laboratory.

TABLE  
Para-sprue, 22 cases  
Showing initial blood count, van den Bergh test, gastric acidity and faecal fat content

Number	Hb in grammes	R.B.C. in millions	Ret. in %	M.C.V. in cu. $\mu$	M.C.H. in $\gamma\gamma$	M.C.H.C. in %	W.B.C. in thousands	E.S.R. in mm. in 1 hour	van den Bergh; bilirubin in mg.	Gastric acidity	PERCENTAGE OF FÆCAL FAT		
											Total	Neutral	Split
1	4.5	1.10	0.3	103.6	41.2	25.2	2.4	..	0.9	Normal	26.0	10.0	16.0
2	11.0	3.64	0.2	97.2	30.5	31.4	8.5	34	Neg.	Do.	22.0	9.8	12.2
3	13.5	3.76	0.2	111.7	35.8	32.1	7.3	18	Do.	Do.	22.0	7.9	14.1
4	9.6	2.56	1.6	117.2	37.6	32.0	6.0	50	0.2	Do.	29.0	10.3	18.7
5	6.6	1.80	0.6	116.6	36.6	31.4	5.0	30	0.4	Pseudo-achlorhydria.	23.7	7.9	15.8
6	12.1	3.80	0.4	102.8	31.8	31.0	7.0	40	Neg.	Normal	24.8	8.2	16.6
7	7.1	2.10	0.8	104.8	35.5	32.5	3.5	20	0.4	Do.	31.9	14.3	17.6
8	11.8	3.46	..	115.6	34.2	29.6	11.0	20	Neg.	Hyperchlorhydria.	31.4	8.2	23.2
9	7.3	2.05	0.2	117.1	35.5	30.4	3.6	40	Do.	Pseudo-achlorhydria.	32.0	8.7	23.3
10	7.1	1.75	1.2	134.2	40.8	30.0	4.4	96	0.3	Normal	27.8	9.2	18.6
11	9.6	2.24	0.4	138.6	42.6	32.0	3.3	38	Neg.	Do.	25.0	12.0	13.0
12	8.8	2.30	0.4	126.1	38.3	30.5	5.5	30	Do.	Do.	33.0	19.2	13.8
13	11.5	3.70	0.3	102.6	31.4	30.4	7.0	20	0.3	Absolute achlorhydria.	29.0	12.3	16.7
14	13.2	3.60	0.2	116.6	36.6	31.4	13.0	30	0.4	Do.	28.7	9.8	18.9
15	10.7	2.90	0.4	117.2	36.8	31.4	5.0	50	0.2	Normal	29.0	9.0	20.0
16	10.7	3.30	0.4	103.0	32.5	31.4	5.0	40	Neg.	Do.	21.3	8.2	13.1
17	12.6	3.70	..	113.5	34.1	30.1	10.0	12	Do.	Pseudo-achlorhydria.	33.2	8.7	24.5
18	12.4	3.16	..	113.9	39.2	33.4	5.3	8	Do.	Normal	25.0	7.2	17.8
19	6.0	1.20	0.4	150.0	50.4	33.6	4.0	8	Do.	Do.	42.0	6.0	36.0
20	13.2	3.90	..	110.2	33.7	30.6	5.0	5	Do.	Pseudo-achlorhydria.	30.0	7.8	22.8
21	6.2	1.64	..	128.1	38.7	30.9	4.9	..	Do.	Do.	21.8	..	..
22	8.8	1.70	..	147.1	51.7	32.0	3.5	20	Do.	Absolute achlorhydria.	22.0	6.0	16.0

liver was invariably followed by a feeling of well-being, increase of appetite and improvement in the blood picture, usually with a sub-maximal reticulocyte response. Besides, 2 patients had marmite, one had nicotinic acid and riboflavin, one had berin injections and 2 had iron by mouth. For achlorhydric patients the following mixture was given after meals with extra water or orange juice, the acid being gradually increased to 1 drachm per dose :—

Dilute hydrochloric acid .. ..  $\frac{1}{2}$  dr.  
Glycerin of pepsin .. .. 1 dr.  
Water to .. .. 1 oz.

Later, constipation was uncommon, but, if present, was regulated satisfactorily by giving isabghul bhusi, one tablespoonful at bedtime with water.

#### Results of treatment

All patients except one had marked clinical improvement; diarrhoea subsided and the tongue became normal. The hæmoglobin increased by more than 5 gm. (up to 8 gm.) in 5 cases, by 2 to 5 gm. in 7 cases and by 1 to 1.5 gm. in 9 cases. The red cells increased by 2 to 4 millions in 6 cases, by 1 to 1.5 millions in 7 cases and by nearly a million in others. The size of

the red cells (M.C.V.) was reduced in all cases. The weight of patients, while in the hospital, increased by 25 to 30 pounds in 2 cases, 10 to 20 pounds in 5 cases and 3 to 8 pounds in the rest, while there was slight loss of weight in 4. One patient was admitted in a deplorable state of health with intractable diarrhoea, and he died. Post-mortem examination was not permitted.

#### An illustrative case

A Hindu male, aged 40 years, a labourer, was admitted with history of chronic diarrhoea (6 to 8 stools a day) for one year. He was thin and anæmic with oedema of the legs. His mouth was sore, the tongue being fissured with a few pigmented patches. The stools were watery and pale yellow with no blood or mucus. No pathogenic organisms were found on repeated examinations. The appetite was poor, and he frequently complained of indigestion and flatulence. The anæmia was macrocytic and hyperchromic, gastric analysis showed pseudo-achlorhydria, and the faecal fat was normal. The progress of the case is shown in the chart (*vide infra*).

#### Summary and discussion

Twenty-two cases of 'para-sprue' have been studied. The condition is fairly common in this country and constitutes a distinct clinical entity. It occurs not only in poor Indians living on a low diet, deficient in good proteins and vitamins, especially of the B<sub>2</sub> complex, but

also in well-to-do people including Europeans and Anglo-Indians. A history of previous dysentery or 'colitis' followed by long-continued semi-starvation diet is common. Chronic watery diarrhoea, loss of weight, sore mouth and nutritional macrocytic anaemia are the outstanding features.

The total faecal fat was normal (within 25 per cent of the weight of dried faeces) in 9 cases, but slightly raised (up to 33 per cent) in 12 cases, while in the remaining one, an Indian patient, a durwan by occupation, it was as high as 42 per cent. The fat was adequately split. (In true sprue, the fat is over 25 per cent and may be 60 per cent, two-thirds of this or more being split.)

In about one-third of these cases there was evidence of poor glucose absorption, the curve being low or flat. [In sprue also, the rise is usually less than 30 mg. and in an appreciable percentage of cases is less than 10 mg. (Napier, 1943).]

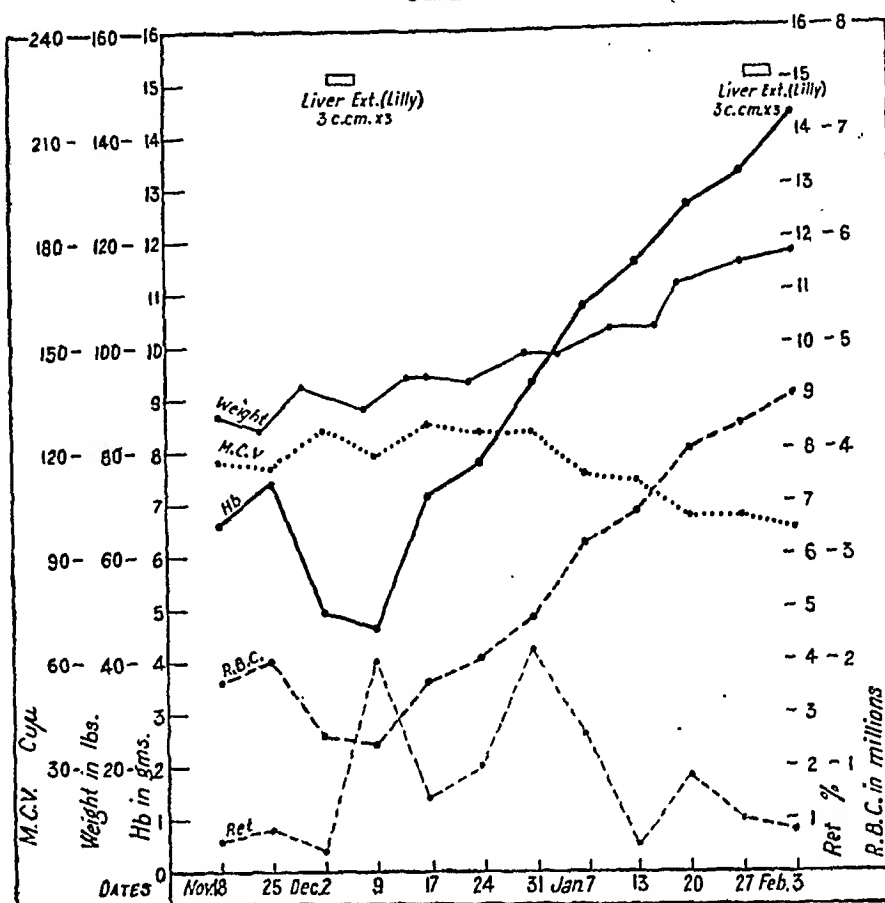
These facts indicate defect in function of the small intestine as in sprue. In most cases the gastric juice contained free hydrochloric acid, but 8 had achlorhydria, being histamin-fast in 3. [Fairley (1930) observed achlorhydria in 14 out of 44 sprue cases, while Hanes (1942) obtained only 21 per cent of histamin-fast achlorhydria.] All had macrocytic anaemia, the average of blood counts being given below along with that worked out by Gradwohl (1938) in a series of 150 cases of sprue.

	Our series	Gradwohl's series of 150 sprue cases
Hæmoglobin in grammes	9.7 (70.5%)	9.7 (66%)
Red cells in millions per c.mm.	2.69	2.71
Cell volume	31.2	33.5
White cells in thousands per c.mm.	5.9	5.3
M.C.V. ..	120.3	123.6
M.C.H. ..	37.5	36.6
M.C.H.C. per cent ..	31.5	26.1

Thus so far as blood picture is concerned it is evident that there is not much difference between the two groups.

These observations would suggest that a small proportion of para-sprue cases have features in common with true sprue, and that border-line cases probably occur.

CHART



Details of a typical case.

The main distinguishing features of para-sprue from sprue are: (i) the racial distribution; it occurs not only among Europeans and Eurasians but also amongst Indians who rarely suffer from true sprue, (ii) the type of diarrhoea, nature of stool and also its chemical composition which differ from those of sprue, (iii) the absence of extreme degrees of emaciation and the peculiar waxy pallor which are often characteristic features of sprue, and (iv) improvement on parenteral administration of crude liver extract without strict dietary regime. Some cases will improve on even normal diet, while graded dieting is essential in sprue.

The word pre-sprue may be applied to this condition, but it should not imply that all cases of sprue begin in this way, or that all of these cases ultimately develop into sprue. The word para-sprue would be a better name. There is however no clear-cut method of diagnosis, but its frequent occurrence in Indians and the watery diarrhoea sometimes with mucus instead of the bulky, pale and frothy stools with high fat content (passed mostly in the morning) are common features that will help to exclude true sprue. The condition appears to be the Indian version of sprue.

In treatment, sulphaguanidine appears satisfactory in stopping diarrhoea, possibly by its action predominantly on the secondary infections



but it was tried in only 5 cases. Parenteral administration of crude liver extracts constitutes the most important specific item. As soon as possible the patients are encouraged to take a liberal diet with first-class proteins and vitamins. Results have been satisfactory, the 21 out of 22 patients having clinical recovery.

*Acknowledgment.*—Our grateful thanks are due to Dr. John Lowe for his helpful suggestions in writing this article.

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### QUININE AND *ALSTONIA SCHOLARIS* (CHHATIM) IN MALARIA A STUDY OF POSSIBLE SYNERGY

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RECENT work has shown that *Alstonia scholaris* has little or no antimalarial action on *Plasmodia* of birds (Goodson, Henry and Macfie, 1930; Buttle, cited by Sharp, 1934), monkeys and man (Mukerji, Ghosh and Siddons, 1942). These findings do not bear out those of earlier workers in the treatment of fevers believed to be of malarial origin. It was claimed that the alkaloids of *Alstonia* were more effective than quinine. Unfortunately, in most of this early work the investigators apparently did not take the precaution of establishing the malarial nature of the fevers they treated by the demonstration of *Plasmodia* in the blood of the patients, with the result that their observations lose in scientific value. These earlier records have been reviewed by Mukerji *et al.* (*loc. cit.*).

In January 1944, the Surgeon-General with the Government of Bengal requested the senior author to investigate the efficacy of a combination of quinine and of 'chhatim' in the treatment of malaria in view of reports that the action of quinine is greatly enhanced by the

addition of 'chhatim'. While the investigation on the synergistic action of 'chhatim' was in progress, Roy and Chatterjee (1944) published a report on their trials with this drug. They found that a dosage of 2 grains of quinine sulphate combined with 'chhatim', given three times a day for about 6 days, is as effective as, or more effective in some respects than, the standard dosage of 5 grains of quinine sulphate thrice daily for 6 days. They used a proprietary preparation of quinine and 'chhatim' in tablet form. The exact composition of the tablets is not stated, but each contains 1 grain of quinine sulphate. The patients had about 6 tablets per day. As their report is a preliminary one, Roy and Chatterjee have not given any details of their observations beyond the temperature chart and parasitological findings of one case as an example. It is interesting to note that they found that 'chhatim' alone had little effect on fever and parasites, confirming Mukerji *et al.* (*loc. cit.*).

#### Methods

Cases of malaria diagnosed as such from clinical and parasitological evidence were treated in three groups: (i) a quinine or control group, treated with 2 grains of quinine sulphate thrice daily for 6 days, (ii) a quinine-'chhatim' or test group treated with 2 grains of quinine sulphate combined with 12 grains of powdered bark of *Alstonia scholaris* of known alkaloidal content, thrice daily for 6 days, and (iii) cases from the quinine group which relapsed and were retreated as in the quinine-'chhatim' group. Parasite counts were made daily from thick films throughout the period of observation of each case. As the counts were often made more than once a day, only the maximum count on each day is noted in this paper to indicate the course of the infections. In the cases showing mixed infection with two species of parasites, it was found difficult to make separate counts for the individual species, but every effort was made to determine the dates on which a species disappeared after treatment and reappeared in the relapse infection. 'Crescent' counts were recorded separately but are omitted from this report because the crescents were not directly affected by either of the treatments. All the cases were male Bengalees. None of the cases included in these groups showed fresh infections with very heavy parasite counts. Most if not all of them had a history indicating malarial infection for several weeks before admission. Moreover, the work was done at a season when fresh infections were uncommon.

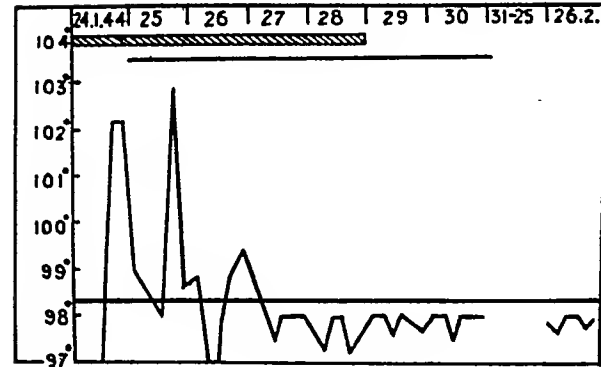
#### Observations

##### (i) Quinine group

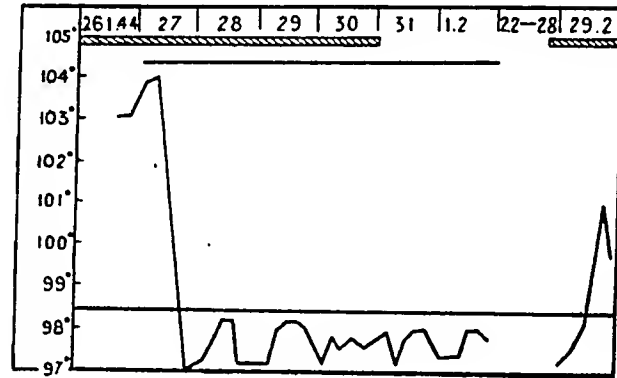
The temperature charts of cases in this group are reproduced in chart 1. The parasitological findings are indicated in table I, commencing with the counts on the first day of treatment.

CHART 1

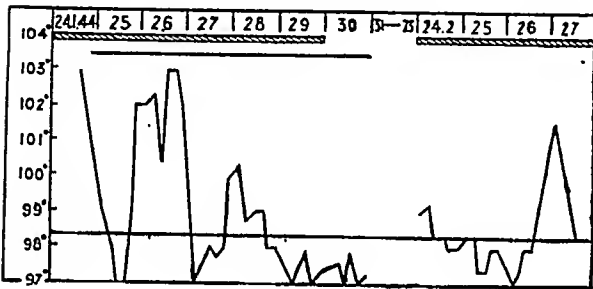
Temperature charts of cases in the quinine group.



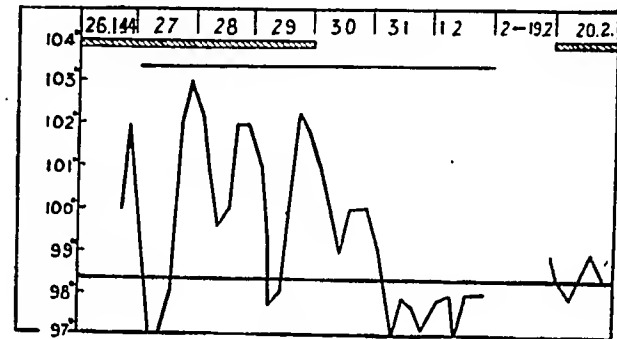
Case 1.



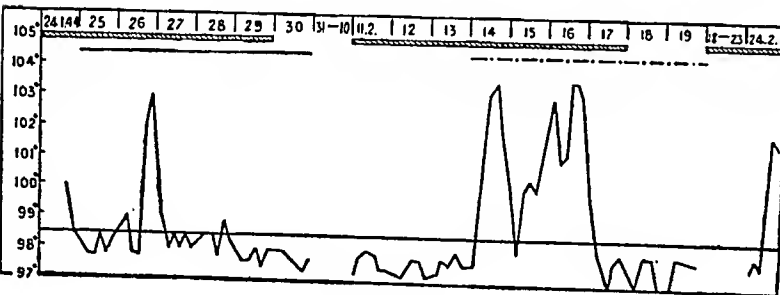
Case 5.



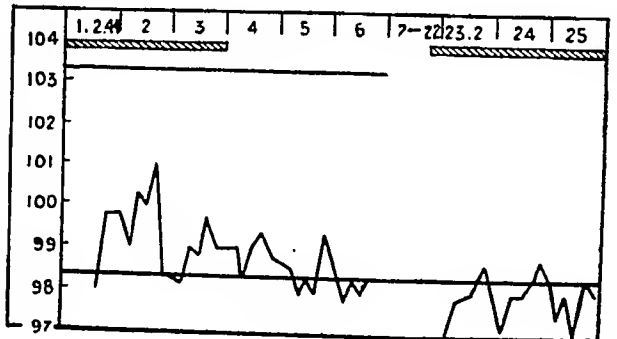
Case 2.



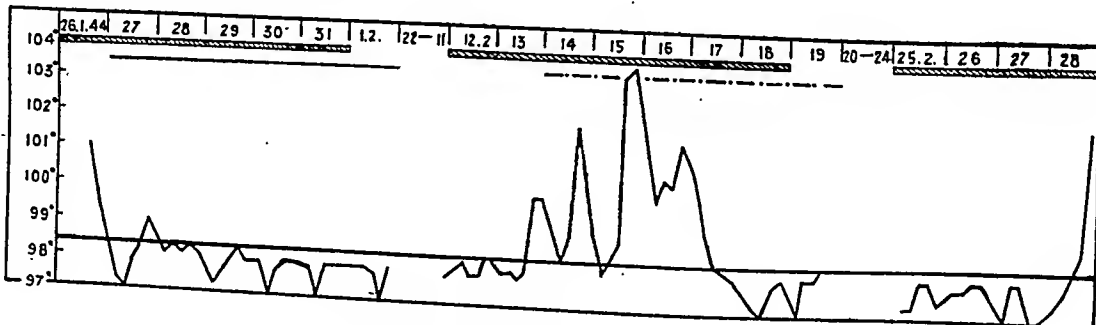
Case 6.



Case 3.



Case 7.



— Quinine  
 - - - Quinine and Chhalim treatment  
 ■ Malaria parasites present

Case 4.

TABLE I  
Parasite counts per c.mm. of blood in the quinine group

Serial number of case	Type of infection	Date of count									
1	<i>P. falciparum</i> and <i>P. vivax</i> .	25-1-44 11,320	26-1-44 38,440	27-1-44 2,120	28-1-44 1,880	29-1-44 to 26-2-44 0					
2	<i>P. falciparum</i>	25-1-44 25,740	26-1-44 7,488	27-1-44 11,664	28-1-44 22	29-1-44 40	30-1-44 to 22-2-44 0	23-2-44 1,070			
3	<i>P. falciparum</i>	25-2-44 8,460	26-1-44 5,520	27-1-44 6,240	28-1-44 120	29-1-44 160	30-1-44 to 10-2-44 0	11-2-44 49			
4	<i>P. falciparum</i> and <i>P. vivax</i> .	27-1-44 10,950	28-1-44 17,160	29-1-44 5,143	30-1-44 1,768	31-1-44 1,200	1-2-44 to 11-2-44 0	12-2-44 136			
5	<i>P. falciparum</i> and <i>P. vivax</i> .	27-1-44 1,260	28-1-44 588	29-1-44 46	30-1-44 13	31-1-44 to 21-2-44 0	22-2-44 58				
6	<i>P. falciparum</i> and <i>P. vivax</i> .	27-1-44 5,408	28-1-44 11,284	29-1-44 240	30-1-44 to 19-2-44 0	20-2-44 38					
7	<i>P. falciparum</i> and <i>P. vivax</i> .	1-2-44 120	2-2-44 36	3-2-44 10	4-2-44 to 18-2-44 0	19-2-44 35					
17	<i>P. malariae</i>	20-5-44 588	21-5-44 420	22-5-44 240	23-5-44 200	24-5-44 76	25-5-44 32	26-5-44 16	27-5-44 12	28-5-44 4	29-5-44 to 14-6-44 Between 0 and 15
											15-6-44 117

Case 1.—Patient, aged 35 years, admitted on 24th January, 1944, complaining of fever with chill and rigor, off and on for the preceding 1½ months. No previous history of fever; slight anaemia; spleen and liver enlarged. Mixed infection of *P. falciparum* (rings and crescents) and *P. vivax* (scanty) present. Treated from 25th January, 1944, to 30th January, 1944. Afebrile after 26th January, 1944 (2 days). Parasites of both species found till 28th January, 1944 (4 days). No clinical or parasitological relapse during 27 days after treatment when the case was discharged.

Case 2.—Patient, aged 16 years, admitted on 24th January, 1944, complaining of fever with chill for the preceding 3 months. Gave history of fever about 4 years previously. Spleen and liver enlarged. *P. falciparum* infection. Treated from 25th January, 1944, to 30th January, 1944. Afebrile after 28th January, 1944 (4 days). No parasites after 29th January, 1944 (5 days). Parasites reappeared 24 days after treatment; fever 3 days later.

Case 3.—Patient, aged 15 years, admitted on 24th January, 1944, complaining of fever off and on for the preceding 2 months; gave history of such fever previously. Slight anaemia; spleen and liver slightly enlarged. *P. falciparum* infection. Treated from 25th January, 1944, to 30th January, 1944. Afebrile after 28th January, 1944 (4 days). No parasites after 29th January, 1944 (5 days). Parasites reappeared 12 days after treatment with fever 3 days later.

Case 4.—Patient, aged 20 years, admitted on 26th January, 1944, complaining of fever with chill and rigor almost every day for the preceding 2 months. Anaemia and slight jaundice; spleen and liver enlarged. *P. falciparum* (rings and crescents) and *P. vivax* (scanty) present. Treated from 27th January, 1944, to 1st February, 1944. Afebrile after 28th January, 1944 (2 days). *P. vivax* not found after 29th January, 1944 (3 days); *P. falciparum* observed till 31st January, 1944 (5 days). Parasites of both species reappeared 11 days after treatment, with fever a day later.

Case 5.—Patient, aged 15 years, admitted on 26th January, 1944, complaining of fever off and on for the preceding 2 months. History of fever 4 months previously, treated with quinine. Slight anaemia; spleen and liver slightly enlarged. *P. vivax* and *P. falciparum* (rings and crescents) present. Treated from 27th January, 1944, to 1st February, 1944. Afebrile after 27th January, 1944 (1 day). *P. vivax* not observed after 28th January, 1944 (2 days). *P. falciparum* not observed after 30th January, 1944 (4 days). *P. vivax* reappeared 21 days after treatment.

Case 6.—Patient, aged 16 years, admitted on 26th January, 1944, complaining of fever off and on for

preceding 5 months. Moderately anaemic; spleen and liver enlarged. *P. falciparum* (rings and crescents) and *P. vivax* present. Treated from 27th January, 1944, to 1st February, 1944. Afebrile after 30th January, 1944 (4 days). Parasites of both species observed till 29th January, 1944 (3 days). *P. vivax* reappeared 19 days after treatment.

Case 7.—Patient, aged 23 years, admitted on 1st February, 1944, having fever almost every day for preceding 1½ months. Spleen and liver enlarged. *P. falciparum* (rings and crescents) and *P. vivax* present. Treated from 1st February, 1944, to 6th February, 1944. Afebrile after 5th February, 1944 (5 days). Parasites of both species present till 3rd February, 1944 (3 days). *P. vivax* reappeared 13 days after treatment.

Case 17.—Patient, aged 20 years. Gave history of fever off and on for 3 months previous to attending the clinic on 19th May, 1944. Spleen palpable. *P. malariae* present. As the patient declined admission into hospital, he was treated from 20th May, 1944, to 25th May, 1944, partly in the laboratory and partly at home. Detailed temperature records could not be obtained. Patient continued with his normal occupation throughout the period of observation. Reported fever on night of 20th May, 1944, and once again on 22nd May, 1944, when the temperature was found to be 102°F. at 4 p.m. No fever experienced after 22nd May, 1944 (3 days). Parasites persisted at a very low level from 24th May, 1944, to 14th June, 1944, when they increased again, though not sufficiently to cause a typical clinical relapse; fever was reported on 15th June, 1944, and next on 26th June, 1944. He was then treated with cinchona febrifuge.

#### Summary of results in the quinine group

(i) Eight cases, all febrile, were treated in this group; one course of treatment controlled the febrile symptoms in every case in 1 to 5 days, average 3 days. A clinical relapse occurred in 7 cases (87.5 per cent), usually a few days after the parasitological relapse.

(ii) *P. falciparum* infection (7 cases) disappeared in all cases after 3 to 5 days, average 4 days, and relapsed in 3 out of 7 cases (42.8 per cent), after periods of 11 to 24 days, average 16 days.

(iii) *P. vivax* infection (5 cases) disappeared in all cases after 2 to 4 days, average 3 days,

but relapsed in 4 out of 5 cases (80 per cent) after periods of 11 to 21 days, average 16 days.

(iv) In view of the large proportion of mixed infections with *P. falciparum* and *P. vivax* in the whole series of 17 cases, it seemed advisable to also study the combined results for cases showing these species; accordingly, in 7 such cases treated in this group, parasites disappeared in every instance in 3 to 5 days, average 4 days, but relapsed in 6 cases (85.7 per cent) after 11 to 24 days, average 17 days.

(v) *P. malariae* (1 case) persisted in very low counts for 21 days when the parasites increased again.

(vi) The consolidated parasitological results for all cases in this group are as follows: after one course of treatment, parasites disappeared in 7 out of 8 cases (87.5 per cent) after 3 to 5 days, average 4 days. Excluding the case (*P. malariae*) in which the parasites persisted after treatment, the relapse rate was 6 out of 7 cases, or 85.7 per cent, parasites reappearing after 11 to 24 days.

#### (ii) Quinine-'chhatim' group

The temperature charts for this group are reproduced in chart 2, and the parasitological data are given in table II.

Case 8.—Patient, aged 26 years, admitted on 5th February, 1944, with oedema of feet. Complained of

11 days after treatment. The patient developed small-pox and had to be transferred to another hospital. Further observation was impossible.

Case 9.—Patient, aged 25 years, admitted on 10th February, 1944, complaining of fever with rigor almost every day for the last 2½ months. History of such fever about 2 years previously. Moderate anaemia; spleen and liver enlarged. *P. falciparum* (rings and crescents) and *P. vivax* present. Treated from 11th February, 1944, to 16th February, 1944. As the attacks continued after this course of treatment owing to the persistence of *P. falciparum*, a second course of the same treatment was given from 22nd February, 1944, to 27th February, 1944. Attacks ceased after 23rd February, 1944 (13 days). *P. vivax* disappeared after 18th February, 1944 (7 days), and *P. falciparum* after 26th February, 1944 (17 days). *P. vivax* reappeared 24 days after the first course of treatment and *P. falciparum* reappeared 13 days after the second course. There was a clinical relapse also.

Case 10.—Patient, aged 35 years, admitted on 17th January, 1944, for oedema. Had a febrile attack with chill and rigor on 25th February, 1944. Similar attacks about 3 months previously. Spleen and liver were not palpable. *P. vivax* present. Treated from 26th February, 1944, to 2nd March, 1944. Afebrile from 26th February, 1944 (2 days) but reappeared 32 days later. The patient left the hospital at night, without the knowledge of the hospital staff, 2 days after the parasites reappeared, so that it could not be ascertained whether he had a clinical relapse at a later date.

Case 11.—Patient, aged 40 years, admitted on 25th February, 1944, complaining of fever with rigor at regular quartan intervals for the last 2 months. History of such attacks off and on for the last year. Spleen palpable and liver slightly enlarged. *P. malariae* infection.

TABLE II

Parasite counts per c.mm. of blood in the quinine-'chhatim' group

Serial number of case	Type of infection	Date of count									
		8-2-44	9-2-44	10-2-44	11-2-44	12-2-44	13-2-44	to 23-2-44	24-2-44		
8	<i>P. falciparum</i> and <i>P. vivax</i> .	48,300	11,160	71,700	17	4		0	30		
9	<i>P. falciparum</i> and <i>P. vivax</i> .	11-2-44	12-2-44	13-2-44	14-2-44	15-2-44	16-2-44	17-2-44	18-2-44	19-2-44	20-2-44
		3,024	1,254	1,632	3,612	4,704	594	6,546	5,520	2,944	364
		21-2-44	22-2-44	23-2-44	24-2-44	25-2-44	26-2-44	27-2-44	to 10-3-44	11-3-44	
		7,344	700	5,120	2,160	2,184	54	0		164	
10	<i>P. vivax</i> ..	26-2-44	27-2-44	28-2-44	to 3-4-44	4-4-44					
		180	6	0		60					
11	<i>P. malariae</i> ..	27-2-44	28-2-44	29-2-44	1-3-44	2-3-44	3-3-44	4-3-44	5-3-44	6-3-44	to 4-4-44
		460	414	288	252	120					
12	<i>P. vivax</i> and <i>P. falciparum</i> (crescents only).	5-3-44	6-3-44	7-3-44	to 11-4-44	12-4-44					
		500	42	0		66					
13	<i>P. falciparum</i>	5-3-44	6-3-44	7-3-44	8-3-44	to 4-4-44					
		490	7,488	132	0						
14	<i>P. falciparum</i>	7-3-44	8-3-44	to 28-3-44	29-3-44						
		11	0		108						
15	<i>P. falciparum</i> and <i>P. vivax</i> .	7-3-44	8-3-44	9-3-44	10-3-44	11-3-44	to 1-4-44	2-4-44			
		55,680	32,344	10,752	1,196	0					
16	<i>P. falciparum</i> and <i>P. vivax</i> .	28-3-44	29-3-44	30-3-44	31-3-44	1-4-44	to 5-4-44	6-4-44			
		5,320	4,032	64	3	0		33			

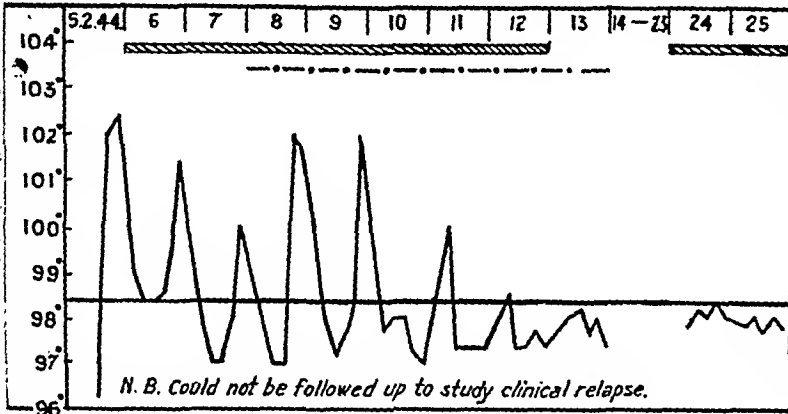
fever with rigor on the 3 preceding days. History of a previous attack of fever 2 months earlier. Spleen and liver not palpable. *P. falciparum* (rings and crescents) and *P. vivax* present. Treated from 8th February, 1944, to 13th February, 1944. Afebrile after 12th February, 1944 (5 days). No *P. vivax* after 10th February, 1944 (3 days); no *P. falciparum* (rings) after 12th February, 1944 (5 days). *P. falciparum* reappeared

Treated from 27th February, 1944, to 3rd March, 1944. Afebrile after 29th March, 1944 (3 days). Parasites not found after 5th March, 1944 (8 days). No recurrence of parasites or fever up to 32 days after treatment, when the patient was discharged.

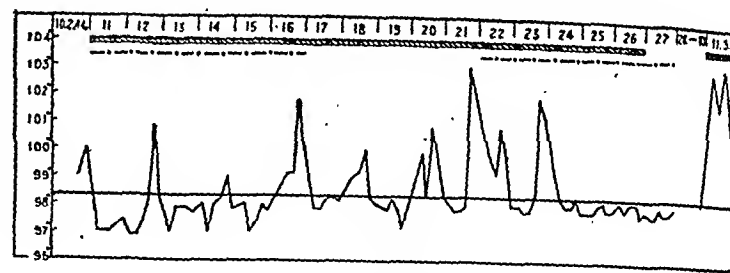
Case 12.—Patient, aged 20 years, admitted on 4th March, 1944, complaining of fever for the past month. Spleen and liver not palpable. *P. vivax* and crescents

# CHART 2

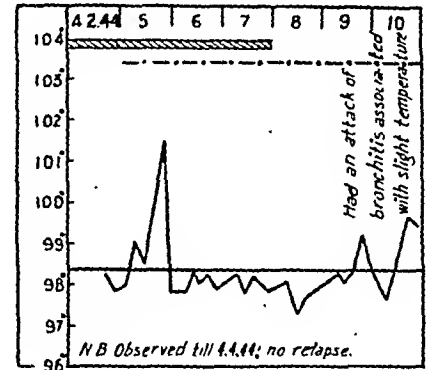
Temperature charts of cases in the quinine-'chhatim' group.



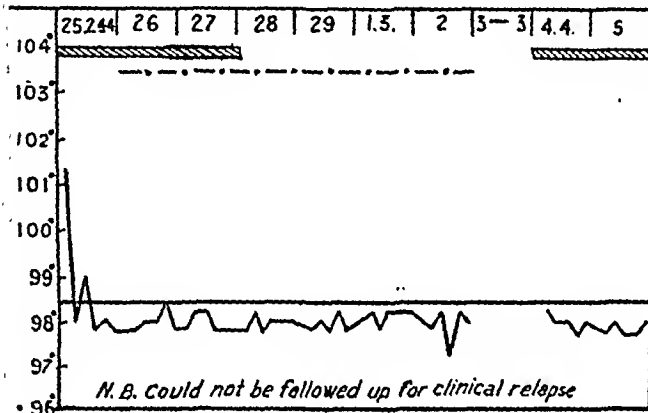
Case 8.



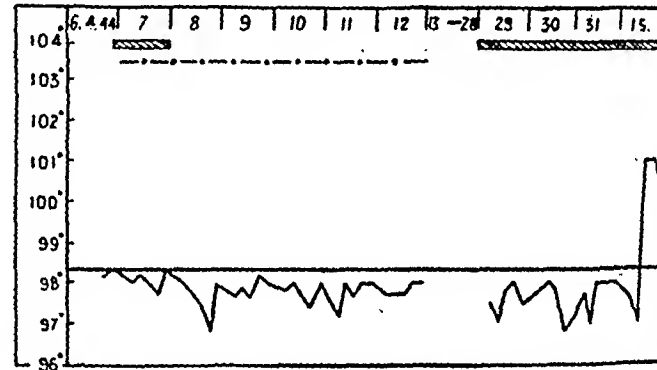
Case 9.



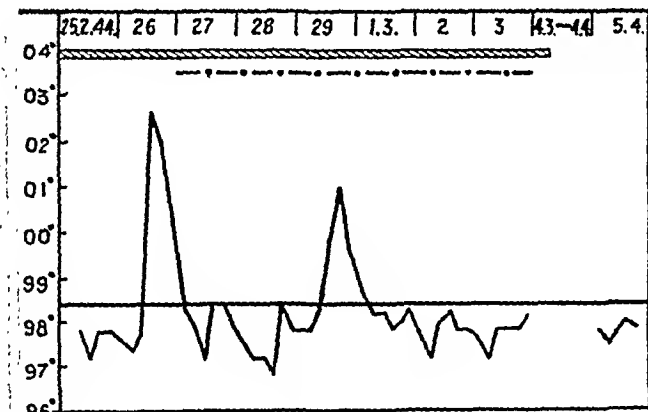
Case 13.



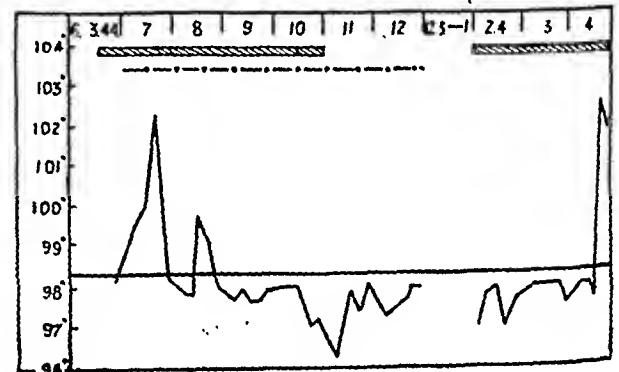
Case 10.



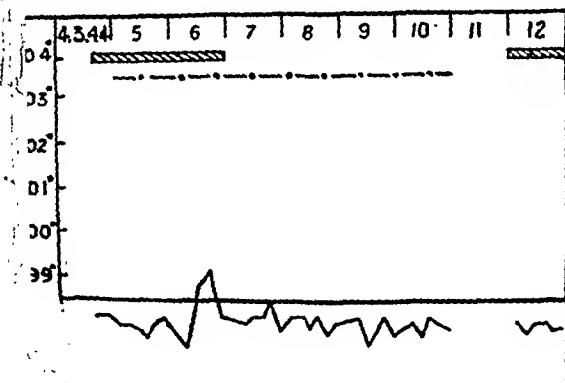
Case 14.



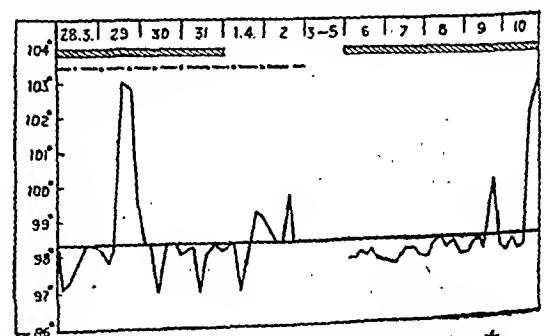
Case 11.



Case 15.



Case 12.



Quinine and 'Chhatim' treatment  
Malaria parasites present

Case 16.

present. Treated from 5th March, 1944, to 10th March, 1944. Afebrile after 6th March, 1944 (2 days). No parasites after same period. *P. vivax* reappeared after 32 days, but decreased spontaneously. There was no evidence of clinical relapse.

Case 13.—Patient, aged 12 years, admitted on 4th March, 1944. No fever at time of admission, but gave a history of attacks 2 months earlier, when he was treated with quinine. Spleen just palpable, liver not enlarged. *P. falciparum* (rings and crescents) present. Treated from 5th March, 1944, to 10th March, 1944. Had a temperature on 5th March, 1944, followed by an increase in the number of parasites next morning. Fever occurred again on 9th March, 1944, and 10th March, 1944, but this was attributed to associated bronchitis. Parasites had disappeared by 8th March, 1944 (3 days). No recurrence of parasites or fever during 48 days after treatment when case was discharged.

Case 14.—Patient, aged 42 years, admitted on 6th March, 1944, complaining of fever off and on for the past 6 months. Quinine treatment taken during this period. Spleen palpable, liver slightly enlarged. Afebrile from date of admission. *P. falciparum* present. Treated from 7th March, 1944, to 12th March, 1944. Parasites not found after first day of treatment, but reappeared 17 days after the course, with fever a few days later.

Case 15.—Patient, aged 20 years, admitted on 6th March, 1944, complaining of fever with rigor off and on for the past 6 months. Slightly anæmic; spleen palpable and liver enlarged. *P. falciparum* (rings and crescents) and *P. vivax* (very scanty) present. Treated from 7th March, 1944, to 12th March, 1944. Afebrile after 8th March, 1944 (2 days). No *P. vivax* after 7th March, 1944 (1 day) and no *P. falciparum* (rings) after 10th March, 1944 (4 days). *P. vivax* reappeared 20 days after treatment; clinical symptoms occurred a few days later.

Case 16.—Patient, aged 16 years, admitted on 25th March, 1944, complaining of fever with chill and rigor daily for the past month. Had fever 3 months previously. Spleen palpable. *P. vivax* and *P. falciparum* (very scanty rings and crescents) present. Treated from 28th March, 1944, to 2nd April, 1944. Afebrile after 2nd April, 1944 (6 days). *P. vivax* not found after 31st March, 1944 (4 days) and *P. falciparum* after 28th March, 1944 (1 day), the latter species reappearing 4 days after treatment, followed by fever a few days later.

#### Summary of results in the quinine-'chhatim' group

(i) Nine cases were treated in this group; 8 of these cases were febrile after admission

to check the paroxysms in one case, in which a second course was necessary. Of 7 cases which were satisfactorily followed up, 4 (57.2 per cent) relapsed clinically.

(ii) *P. falciparum* was controlled by one course of treatment in 5 out of 6 cases (83.3 per cent), disappearing after 1 to 5 days, average 3 days; 4 out of 6 cases (66.7 per cent) relapsed with this parasite after 4 to 17 days, average 11 days.

(iii) *P. vivax* disappeared in all 6 cases after 1 to 7 days, average 3 days; 4 cases (66.7 per cent) relapsed after 20 to 32 days, average 27 days.

(iv) Combining the results for cases showing *P. falciparum* and *P. vivax* as in the quinine group, it is found that after one course of treatment parasites disappeared in 7 out of 8 cases (87.5 per cent) in 1 to 5 days, average 3 days; 7 cases relapsed (87.5 per cent) after 4 to 32 days, average 18 days.

(v) *P. malariae* (1 case) disappeared after 8 days and did not reappear up to 32 days after treatment.

(vi) The consolidated parasitological results for all cases in this group are as follows: one course of treatment controlled the parasites in 8 out of 9 cases (88.8 per cent) in 1 to 8 days, average 4 days; 7 out of 9 cases (77.8 per cent) relapsed after 4 to 32 days, average 20 days.

#### (iii) Relapse cases from the quinine group re-treated in the quinine-'chhatim' group

The two cases in this group were nos. 3 and 4. Their temperature charts after re-treatment are shown in chart 1 and the corresponding parasitological data in table III.

Case 3 was re-treated from 14th February, 1944, to 19th February, 1944. Afebrile after 17th February, 1944 (4 days). *P. falciparum* not found after 17th February, 1944 (4 days), but reappeared 5 days after re-treatment.

Case 4 was re-treated from 14th February, 1944, to 19th February, 1944. Afebrile after 17th February, 1944 (4 days). Parasites

TABLE III  
Parasite counts per c.mm. of blood in cases from the quinine group which relapsed and were re-treated as in the quinine-'chhatim' group

Serial number of case	Type of infection	Date of count							
		14-2-44	15-2-44	16-2-44	17-2-44	18-2-44 to 23-2-44	24-2-44		
3	<i>P. falciparum</i>	16,848	22,200	4,000	416	0	204		
4	<i>P. falciparum</i>	27,000	36,708	13,112	2,310	18	0	24-3-44	25-3-44
									19

into hospital and before treatment was begun. One course of treatment controlled the febrile symptoms in 7 out of 8 cases (87.5 per cent) after 1 to 6 days, average 3 days, but failed

(*P. falciparum* and *P. vivax*) disappeared after 18th February, 1944 (5 days), only to reappear (*P. falciparum*) 5 days after the course of quinine and 'chhatim'.



### Discussion

There appears to be no significant difference between the results obtained with the treatments consisting of 6 grains of quinine daily, and of 6 grains of quinine plus 'chhatim' daily. In such small groups of cases (8 and 9 cases) differences in results would have to be very marked before they were significant. From some aspects, such as control of clinical attacks in *P. falciparum* infections, the results in the quinine group are slightly better; from others, such as parasite relapse rate, especially for *P. vivax*, and the period before a relapse with the latter species, the results are slightly better in the quinine-'chhatim' group. Only the clinical relapse rate is appreciably lower in the quinine-'chhatim' group, but the validity of this finding for comparative purposes is questionable, firstly because the groups are so small that such differences are not statistically significant and secondly because 2 out of 7 cases which had a parasite relapse could not be followed up to determine whether a clinical relapse also occurred. It will be observed that in most instances parasites could be detected a few days before the clinical relapse.

The results in the cases which relapsed after quinine treatment and were re-treated as in the quinine-'chhatim' group add nothing in favour of 'chhatim'. The preceding remarks refer mainly to *P. falciparum* and *P. vivax* infections, for too few cases of quartan malaria have been studied to draw conclusions in respect of *P. malariae*.

A point which deserves notice is that the cases in the quinine group had comparatively heavy parasitic infections; thus 50 per cent gave counts exceeding 10,000 parasites per c.mm. as against 22 per cent in the quinine-'chhatim' group. In spite of this, the results in the latter group are not correspondingly better, suggesting that 'chhatim' exercised no appreciable synergistic action on quinine.

### Summary

In view of reports that *Alstonia scholaris* ('chhatim') greatly enhances the action of quinine in the treatment of malaria, so that a comparatively small dosage of the quinine suffices to effect a cure, a study was undertaken of the synergistic action of 'chhatim'. Seventeen cases of malaria, all of several weeks' duration, were treated in two main groups: (i) a quinine or control group of 8 cases treated with 2 grains of quinine sulphate t.d.s. for 6 days, (ii) a quinine-'chhatim' or test group of 9 cases treated with 2 grains of quinine sulphate combined with 12 grains of powdered bark of *Alstonia scholaris* of known alkaloidal content t.d.s. for 6 days. The efficacy of the two treatments was studied by both clinical and parasitological methods. There was no significant difference between the results obtained in the two groups, suggesting that 'chhatim' exercises no synergistic action on quinine. It was found

that 2 grains of quinine sulphate t.d.s. for 6 days controlled both fever and parasites in a large proportion of cases, but relapses after short periods were very common. There is, therefore, hardly any justification for using such small doses of quinine in the treatment of malaria. In fresh cases of malignant tertian infections particularly it would actually be unsafe to rely on this small dosage, in that one cannot judge the seriousness of the disease by examination of the peripheral blood smears alone; nor can one foretell which case will take a serious turn. Perhaps from these and other considerations, the Malaria Commission of the League of Nations (1937) suggested a dosage schedule of 5 grains t.d.s. for 5 to 7 days in the treatment of malaria.

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[Note.—Our experience confirms the opinions expressed in this paper. In chronic and relapsing malaria with relatively low-grade infections, the fever can often be controlled by doses of quinine as low as 6 grains a day; the addition of 'chhatim' appears to make little if any difference. With fresh infections of malaria, which are usually of much higher grade, the use of such small doses is often of little use and actually dangerous. In one case of heavy infection with *P. falciparum* seen by the editor, quinine and 'chhatim' used as described above completely failed to control the fever and the patient died. In other similar cases, the treatment had to be abandoned for a larger dose of quinine, which controlled the fever.

Even if the fever is controlled with these small doses of quinine, with or without 'chhatim', the relapse rate is so high that further courses have to be given, and ultimately there is no saving of quinine. We fear therefore that the attempt to make quinine supplies go further, by using small doses in combination with 'chhatim', are not likely to meet with much success, and moreover have certain very real dangers.

Both the above paper and that of Roy and Chatterjee deal with cases treated at the end of the malaria season, and mostly with cases of several weeks' duration with only what amounts to a residual low-grade infection. If the work had been done in the malaria season on cases of heavy fresh infection, the results of treatment would, we feel, have been very different.—EDRON, J. M. G.]

### MACROCYTIC ANÆMIA

#### THE UNKNOWN HÆMOPOIETIC FACTOR IN WHOLE LIVER AND YEAST

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CASES of macrocytic anæmia that resist parenteral liver and marmite but yield to whole liver or yeast are now reported by various

workers all over the world. As far back as 1938 Napier and his co-worker reported that macrocytic anæmias in the tropics including those of pregnancy could be grouped on therapeutic grounds as (a) curable with refined liver extract such as anahæmin, (b) curable with crude liver extracts or marmite, and (c) curable with campolon. We now see that a fourth group which resists even campolon but yields to whole liver or yeast is added to the list. However, the anti-anæmic substance that is missing from or not present in sufficient quantity to be active in crude and refined liver extracts, but is present in whole liver and yeast, has not yet been identified. The purpose of this communication is to produce clinical evidence to suggest the probable identity of this unknown hæmopoietic factor, and to show that, in such refractory cases, deficiency of nicotinic acid exists and at a certain stage of the illness reaches a definite degree of intensity at which the anæmia and other associated conditions defy all treatment with parenteral liver, marmite and high protein diet unless the deficiency is met by exhibition of pure nicotinic acid or its rich sources, whole liver or yeast. I give below a few illustrative cases from my records in support of my view.

*Case 1.\*—*A man had acute diarrhoea and vomiting in 1936 which persisted in sprue-like form with severe anæmia for a year and was relieved with a course of torantil, abidol and campolon. He had a relapse in 1939. Old remedies failed and his anæmia resisted intensive therapy with campolon, betaxin and other drugs. Nicotinic acid deficiency was suspected and the additional therapy tried.

*Condition of circulatory system before nicotinic acid.*—R.B.C. 2.9 millions, Hb 90 per cent, C.I. 1.5, W.B.C. 5,312 and a blood picture of megalocytic hyperchromic anæmia. B.P. 92/50. Dyspnoea, rapid pulse, weak and dilated heart with bruit and swelling of whole body present. Expected to die at any moment.

*After nicotinic acid therapy.*—R.B.C. 3.15 millions, Hb 90 per cent, W.B.C. 13,125, size of R.B.C. normal. B.P. 110/70. Edema disappeared, heart became normal and he began to walk about, and all in 20 days. He gained 42 lb. in 2 months. No relapse for 4 years.

The response was so rapid and complete that I could not help believing that nicotinic acid had some unknown properties to quickly regenerate the depressed hæmopoietic system.†

*Case 2.*—A man was admitted into our hospital in 1940 with fever, extreme degree of anæmia, dyspnoea, palpitation and troublesome indigestion. He had similar attacks in 1929, 1933 and 1939. He received 44 c.cm. of campolon with great benefit during the third attack. Resisted all injections, tonics and hæmatins during the fourth attack. Nicotinic acid was not available. Yeast, raw liver juice and high protein diet were prescribed.

*Condition before the treatment.*—Macrocytic anæmia with R.B.C. 1.7 millions, Hb 45 per cent, C.I. 1.3, W.B.C. 9,000, polymorphonuclears 40 per cent, lymphocytes 58 per cent. Anisocytosis and poikilocytosis present. B.P. 90/45. No ankylostoma or any other ova in the stools. Van den Bergh negative. Achlorhydria on fasting and after porridge meal.

*Condition after the treatment.*—R.B.C. 3.58 millions, size of R.B.C. 7.8 $\mu$ , Hb 55 per cent. Anisocytosis and poikilocytosis not present. B.P. 115/65. HCl returned in gastric juice. Clinically cured and remained so when examined after a year. No relapse now for last 3 years.

The anæmia in this case resisted liver injections but responded to liver by mouth and yeast. The response, however, was not so rapid as with nicotinic acid.

*Case 3.*—A female had gastro-intestinal troubles and severe anæmia starting after child-birth. She suffered for 4 years. Hundreds of iron, liver and calcium injections with other drugs were given without any effect. She became pale, weak and emaciated and then suddenly developed cramps in the legs and pain in the abdomen. She gasped for breath and appeared to be dying. Signs of intense anæmia and acute depletion of nicotinic acid were present. She was given 10 c.cm. hepatex with 50 mgm. of nicotinic acid in 20 c.cm. of 25 per cent glucose intravenously. Her abdominal pain lessened and cramps disappeared immediately. A full course of nicotinic acid with other appropriate treatment was then given.

*Condition before nicotinic acid.*—R.B.C. 1.2 millions, size of R.B.C. 8.5 $\mu$ , Hb 22 per cent, BP 80/45. Stool showed no ova, no cyst, no ankylostoma and no characteristics of sprue. X-ray revealed extreme enteroptosis and no other abnormality.

*Condition after nicotinic acid.*—R.B.C. 3.5, size 7.5 $\mu$ , Hb 75 per cent. She was able to walk about in a week and could do a mile without fatigue in a month. She became clinically normal but often had 2 to 3 stools a day after some indiscretion in food. She has remained well for 3 years.

*Case 4.*—Female, aged 21 years. Pseudo-pernicious anæmia of pregnancy successfully treated with parenteral liver and blood transfusions during first and second pregnancies. Third ended in an abortion and fourth in still birth after which the anæmia became refractory to parenteral liver and three blood transfusions. I gave 28 c.cm. of refined liver extract, 44 tablets of fersolate with marmite and a liberal diet. There was no response. I then gave 25 c.cm. of campolon and 18 mgm. of berin in 9 days. There was a slight improvement, R.B.C. rising from 1.2 millions to 1.5 millions. I then tried 300 mgm. of nicotinic acid intravenously given in 10 days. The response and recovery were dramatic.

*Condition under refined and crude liver extracts, marmite and iron.*—R.B.C. 1.2 millions, size 8.1 $\mu$ , Hb 30 per cent, C.I. 1.25. Edema of feet and eyelids. Râles and rhonchi in lungs, severe cough, extreme weakness and restlessness. Wassermann negative in husband and wife.

*Condition under nicotinic acid.*—R.B.C. 3.8 millions, size 7.8 $\mu$ , Hb 70 per cent, C.I. 0.9. She became normal but took liver soup and nicotinic acid tablets as maintenance treatment for 6 months. She has been well for 3 years.

*Case 5.*—A male, aged 24 years, had gastric pain, tender sigmoid and severe anæmia for 6 months. He became bed-ridden and was admitted into a railway hospital on 23rd October, 1940.

No history of dysentery; no ova or cyst in the stool; no albumin or sugar in urine; he was given a course of emetine, santonin, liver extract intramuscularly and iron, arsenic and nux vomica mixture and a milk and sage diet for 20 days by my colleague. There was no relief. His stool was again examined on 4 successive days but no ova, cyst or ankylostoma found. He was then given 2 c.cm. of hepatex injection daily and 30 grains of ferri et ammoni citras and 1 drachm of dilute HCl 3 times a day with suitable diet for 10 days which gave no relief whatsoever.

I then took the patient in hand. He gave a history of dyspepsia for 6 years. Constipation, tympanitis and epigastric pain gradually getting worse, nausea and vomiting in the morning and, later, during the day for a few months. Patient was very weak, pale and anæmic and positively 'mental' with disturbed dreams. Knee jerks absent. Lungs normal. B.P. 84/40. R.B.C. 1.8 millions, size 8.4 $\mu$ , Hb 40 per cent, C.I. 1.1. Nothing

\*Details of case 1 will be found in J. I. M. A., 12, 1, and of others in Patna Journ. Med., 17, 1.

†In this case the anæmia apparently persisted but did not remain megalocytic.—Error, I. M. G.

in stool and urine. Weight 76½ pounds. Achlorhydria on fasting and after porridge meal. Nicotinic acid intravenously was intentionally not given to see the effect of parenteral liver extract plus marmite and high protein diet. He was given 4 c.cm. of hepatex intramuscularly on alternate days and a liberal diet with marmite plus one drachm of dilute HCl and ½ drachm of ferri et ammon. cit. 3 times a day for 10 days, with the result that his R.B.C. went down from 1.8 millions to 1.6 millions, his weight did not increase but his Hb rose from 40 to 60 per cent. I then ordered 10 c.cm. campolon first day and 5 c.cm. on third, fifth and eighth day with 2 mgm. of berin intramuscularly every day. Iron and HCl remained the same. Pepsin was given after meals. His diet was 1 cup of orange-juice at 6 a.m., 2 lightly boiled eggs, 2 biscuits, 1 cup of milk with ovaltine and marmite at 8 a.m., vegetable or meat soup, minced chicken, light pudding, marmite and fruit-juice at 12 a.m. A cup of milk with ovaltine if required at 4 p.m. and a soup, a meat or fish dish, marmite and pudding at 8-30 p.m. His Arneth count pointed to a septic focus for which a sulphonamide intramuscularly was tried. After 2 weeks of this intensive dietetic, medicinal and parenteral liver therapy the result was swelling of his feet and face. His urine was still normal. After 3 weeks his R.B.C. was 1.6 millions, size 8.2μ, Hb 50 per cent, W.B.C. 3,120, polymorphonuclears 80 per cent, lymphocytes 18 per cent, monocytes nil, eosinophils 2 per cent, poikilocytosis present, œdema of feet, legs and face increased, vomiting very troublesome. Positive signs of nicotinic acid deficiency appeared. Weight not increased.

All medicines were then stopped to see the effect of nicotinic acid therapy; the diet continued to be the same. Fifty mgm. of nicotinic acid in 25 c.cm. of 25 per cent glucose intravenously on alternate days and then every fourth day up to sixth injection was given. The response was rapid. His blood on 28th December, 1940, showed R.B.C. 2.6 millions, Hb 70 per cent, size of R.B.C. 7.8μ, W.B.C. 8,426, polymorphonuclears 71 per cent, lymphocytes 24 per cent, eosinophils 5 per cent. He was given 10 injections in a month. Œdema disappeared. HCl after porridge meal returned. Discharged to duty on 17th January, 1941, as much improved. His blood on 31st March, 1941, was R.B.C. 3.22 millions, size 7.0μ, Hb 55 per cent, B.P. 95/55, weight 78½ pounds. His weight after 6 months was 81½ pounds, and blood almost normal. His weight after a year was found 93½ pounds and blood normal. He still takes a cup of liver soup twice a week and has been well for 3 years.

*Comment.*—The anaemia resisted parenteral liver during the second and fourth attack in cases 1, 2 and 4 and in the late stages of the first attack in cases 3 and 5 when signs suggestive of secondary pellagra could be detected in case 1 and of a pre-pellagrous condition in cases 2 and 4 and very faint suggestions of deficiency in cases 3 and 5. These facts suggest that the resistance to parenteral liver developed only when nicotinic acid deficiency reached a definite degree of intensity.

A careful study of the clinical features of other workers' cases also shows probable signs of nicotinic acid deficiency. In Bagchi's 94 cases (1943) 27.5 per cent had diarrhoea and 10 per cent had soreness of the mouth. Of the three cases of Fullerton (1943) one had burning pain in the tongue and superficial ulcer on its each margin and the second had diarrhoea and pain in the tongue and even atrophy of tongue papillae. Thirty-three per cent of Taylor and Manehanda's cases (1940) had soreness of the tongue and 25 per cent had actual glossitis.

Case 5 effectively demonstrated that nicotinic acid gave a rapid hæmopoietic response independently of whole liver and yeast when parenteral liver, marmite and high protein diet totally failed. I have no doubt that these cases would have been taken to have marrow aplasia and if nicotinic acid in some form or other was not given to them they would have proved fatal.

*Discussion.*—According to Castle's theory, macrocytic anaemias are caused by (a) deficiency of extrinsic factor in the food, (b) permanent or temporary failure of secretion of intrinsic factor in the stomach, (c) deficiency of both the factors, (d) interference with the combination or absorption of the hæmopoietic principle formed by both the extrinsic and intrinsic factors. Liver was first found to give marvellous results in true Addisonian and other macrocytic anaemias. Castle's extrinsic factor was then available in the form of marmite and nutritional anaemias like 'tropical macrocytic anaemia' yielded to it favourably. McRobert, Reddy and Subramanian (1940) reviewing 100 cases of anaemia admitted into the General Hospital, Madras, found 7 cases of macrocytic type, 6 of which were achlorhydric. They all yielded to marmite. Napier (1936) and others also reported good results with marmite in such cases. It has thus been commonly believed that macrocytic anaemias respond favourably to adequate parenteral liver and marmite, and that a case not responding to intensive and extensive therapy of such a kind is supposed to have marrow hypoplasia, and to show a grave prognosis. This outlook has been responsible for a very high mortality specially amongst the cases of severe type of macrocytic anaemia of pregnancy. Bagchi (1943) giving an analysis of 107 cases of anaemias in pregnancy treated in the Carmichael Medical College Hospitals, Calcutta, noted that in as many as 104 cases, the anaemia could not be attributed to any cause outside pregnancy, and that 94 of them belonged to hyperchromic-orthochromic varieties of tropical macrocytic and pseudo-pernicious anaemia of pregnancy. The treatment given was intensive iron and parenteral liver therapy with intramuscular injection of whole blood, plus a liberal diet and blood transfusion when necessary. The mortality in 74 of his cases was 24 per cent, and in 14 of his severe cases was as high as 43 per cent, showing that some very potent factor was missing from the line of the recognized routine treatment. Miller and Studdert (1942) draw attention to 5 Newcastle cases which failed to show any significant response to normal diet plus marmite and refined and crude liver extracts but responded to raw liver by mouth. Davidson, Davis and Innes (1942) give details of 16 cases of macrocytic anaemia of pregnancy, 10 of which did not yield to massive doses of liver extract. Two of them proved fatal while ultimate response was

obtained in 8 cases when iron, yeast and ascorbic acid were added to the treatment and life was maintained by blood transfusions during the refractory period. Fullerton (1943) records 3 cases of macrocytic anæmia of pregnancy which proved refractory to intensive parenteral liver but yielded rapidly to whole liver. Fullerton believes that there are some unknown anti-anæmic factors in the whole liver that act so rapidly in such refractory cases. I would like here to emphasize that in Davidson, Davis and Innes' (1942) 8 refractory cases whole liver was not given but it was probably yeast that ultimately gave the satisfactory results. The unknown factor, therefore, appears to be common to both the whole liver and yeast. In discussing macrocytic anæmias other than those of pregnancy, Davidson (1939) recorded a case of macrocytic anæmia associated with steatorrhœa which did not respond to parenteral liver extracts alone but did so when high protein diet including  $\frac{1}{2}$  pound of whole liver was added to it. Davidson tends to attribute the response to high protein diet, but Fullerton (1943) appears to suggest, and I agree with him, that the improvement in Davidson's case was probably due to the inclusion of  $\frac{1}{2}$  pound of whole liver daily to the high protein diet. Taylor and Manchanda (1940) treated 24 cases of 'tropical macrocytic anæmia' with parenteral liver, marmite and yeast and lost only one case—a mortality of 4.2 per cent. They, however, failed to understand why two of their cases remained macrocytic for two and three months and did not yield to 'intensive treatment by liver injections, marmite and blood transfusion'. They apparently did not give yeast to these two of their cases. Ungley and James (1934) reported that, in 10 of their 18 cases, massive doses of yeast extract given by mouth produced a hæmopoietic response but the same extract given parenterally did not. Napier (1936) also found that yeast extract given by mouth cured tropical macrocytic anæmia and noted (1939) that a yeast extract given even parenterally appeared to have a curative effect in one of his cases. Napier (1936) finding cases resistant to routine treatment put forward an idea that tropical macrocytic anæmias might be due to the deficiency of an 'independent hæmopoietic principle' and later on (1939) believed that it was not identical with Castle's extrinsic factor. Fairley and his co-workers (1938) had sufficient evidence to divide their cases of tropical macrocytic anæmia into hæmolytic and non-hæmolytic group. Napier and Majumdar (1938), supporting that view, came to the conclusion that macrocytic anæmia may be produced by a 'relative deficiency in important food factor probably associated with vitamin B<sub>2</sub> complex' and that this deficiency may be determined by excessive hæmolysis in an individual on a border-line diet due to malaria or other similar conditions. Napier (1939) came very near the truth when he definitely

stated that such cases may be due to a deficiency in B<sub>2</sub> complex and that yeast and crude liver probably contain his 'additional hæmopoietic factor'. He, however, failed to identify the deficient substance but in order to get it identified he very rightly suggested that 'careful quantitative work with only purified fractions of autolyzed yeast and liver extracts seems to offer the best prospects'. For the last 4 years I have been using nicotinic acid in the treatment of refractory cases of macrocytic anæmia associated with pregnancy, pellagra, steatorrhœa and other conditions, with almost dramatic results. The short notes of the illustrative cases cited above, the details of some of which have already appeared in other journals, show that nicotinic acid can act independently of liver and yeast. It will thus be seen that not only the macrocytic anæmia of pregnancy but of all varieties may prove at one time or other refractory to parenteral liver, marmite and high protein diet but yield to whole liver, yeast or nicotinic acid. As these three substances have given satisfactory results independently in different hands, and as whole liver and yeast are both very rich sources of nicotinic acid, I am inclined to believe that nicotinic acid is the factor, or one of the essentially active factors, which really acts when cases refractory to parenteral liver and marmite respond to whole liver or yeast, and which Fullerton believed to be present in the whole liver and Napier in autolyzed yeast. It may, however, be noted that this resistance to parenteral liver generally develops either late in the first attack or at some time during the recurrence of the disease. It is, therefore, justifiable to assume that it is the depletion of nicotinic acid which at a certain stage and intensity interferes either with the secretion of the intrinsic factor or with the combination of it with the extrinsic factor and makes a case refractory to ordinary therapy. Nicotinic acid is now recognized to be responsible for the maintenance of growth, health and nourishment of epithelial tissues in the body. Its deficiency as noted in pellagrins causes atrophic type of degeneration of epithelial cells. It is, therefore, not difficult to see how it could affect the gastric function and the secretion of gastric hydrochloric acid and Castle's intrinsic factor, and how it could interfere with the combination and absorption of the hæmopoietic principle in the gastro-intestinal tract. The meagreness and limitations of my clinical work and observations are obvious, but the research has been done with a definite purpose in view and in as scientific and systematic a manner as possible. Further work with nicotinic acid in such cases by those who have better facilities is, therefore, clearly indicated.

*Summary.*—Clinical evidence has been brought forward to prove that nicotinic acid deficiency may occur in cases of macrocytic anæmia associated with pregnancy or with any other condition, and that nicotinamide depletion

in the body can reach a stage when the supply of known anti-anæmia factors, in the form of parenteral liver extract and marmite, cannot produce blood regeneration; in such cases the exhibition of nicotinic acid singly or in combination with other routine treatments may act almost in a dramatic fashion in bringing the blood picture to normal.

It is suggested that nicotinic acid is the factor that acts when cases refractory to parenteral liver rapidly yield to whole liver or yeast.

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### LATENT TUBERCULOSIS IN MEDICAL STUDENTS OF THE KING EDWARD MEDICAL COLLEGE, LAHORE, PUNJAB

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WITH the interest in mass miniature radiography in India, this report is submitted for publication, in an incomplete state. The work was interrupted by recall to military service.

The work was planned for a five-year period with a follow-up of positive cases.

For 3 years from 1938 to 1940, medical students of the King Edward Medical College, Lahore, India, were subjected to yearly examination by the intradermal injections of international standard tuberculin solutions of 1/1,000 strength, which had been freshly prepared. The technique used was the standard one of the Tuberculosis Association of India based on the Mantoux reaction. In some cases negative-reacting students were re-examined with a 1/100 solution. Full-size skiagrams of the chests of the first-year medical students were

taken during their first year of college attendance. Those with positive films were subsequently investigated clinically, and, where necessary, frequent later skiagrams were taken.

The students were Moslem, Sikh and Hindu, their numbers being according to the communal representation of the province.

The results of the Mantoux reactions obtained are shown in table I.

The following conclusions and observations were made:—

(1) On admission to the college, students gave a high rate of positive Mantoux reactions, 51 per cent of the total first year in 1939 and 68.5 per cent in 1940 being positive. High rates had been obtained among Lahore school children.

(2) The incidence of positive reactors rose in the fifth-year medical students to 86 per cent in 1938 and 98 per cent in 1939.

(3) The largest rise in the percentage of positive reactions took place between the third and fourth years, when students begin work in the medical, surgical and tuberculosis wards.

(4) No cases of radiologically or clinically active tuberculosis developed during this period in the students who developed a positive Mantoux reaction after being earlier negative. Skiagrams of the chest of such students were taken as a routine. It is now a commonplace that primary tuberculosis is, in the vast majority of people, of the mildest nature and is often not accompanied by clinical signs or symptoms. These students were unaware of any illnesses, though some complained of coughs and colds.

(5) Twenty students who had shown positive reactions later showed negative ones. This change is recorded in the literature of the Mantoux reaction. Its significance is not fully understood.

(6) Fifteen per cent of the positive reactions were of the severe +++ or ++++ type (with ulceration). These reactions led to much discussion, but no conclusions were reached.

The results of the skiagrams of the chest are shown in table II.

Looking back on this work, I now think that the interpretation of the group 'positive skiagrams without toxæmia' may need revision in future work of this nature. It is notoriously difficult to interpret films of early chest tuberculosis. There may have been an inclination towards reporting positive findings when now, with more experience, negative results would be reported. But in two students in whom active clinical tuberculosis in fact developed in 1940, the early radiological signs at the apices of the films had been missed at the first examination when the students were examined in an apparently healthy state in 1938. Subsequent examination of the first films (1938) showed early disease.

On admission to the college, students were medically examined, but this examination did



TABLE I  
*Results of Mantoux examinations*

Year students	1938			1939			1940		
	Total examined	MANTOUX POSITIVE		Total examined	MANTOUX POSITIVE		Total examined	MANTOUX POSITIVE	
		Number	Per cent		Number	Per cent		Number	Per cent
First-year ..	62	38	61	82	42	51	73	50	68.5
Second-year ..	58	42	72	70	49	70	81	52	64
Third-year ..	74	56	76	62	43	70	54	40	74
Fourth-year ..	66	57	86	82	68	83	57	48	84
Fifth-year ..	59	51	86	43	42	98	57	49	86
TOTAL ..	319	244	77	339	244	73	322	239	74.2

TABLE II  
*Results of skiagram of chest of first-year students*

Year	Total examined	Positive skiagrams with toxæmia*	Positive skiagrams without toxæmia	Total positive skiagrams	Doubtful skiagrams
1938-39 ..	86	2=2.3%	8=9.3%	10=11.7%	3=3.5%
1939-40 ..	99	1=1.0% as before	8=8.9%	9=11.0%	4=4.4%
1940-41 ..	86	3=3.5%	4=4.0%	7=8.1%	1=1.2%
TOTAL ..	271	6=2.2%	20=7.3%	26=9.9%	8=2.9%

\* Toxæmia indicates one or more of the following—a raised blood sedimentation rate, a slight rise of temperature or pulse rate, or loss of weight.

not include a chest skiagram. Skiagrams were taken during the first year at the college.

Every effort was made to keep suspected cases under clinical and radiological observations, without unnecessarily worrying the students, sometimes a difficult problem!

Observations of the same kind were made on nurses of the Mayo Hospital, Lahore, with similar results.

Although this work was not completed, the following conclusions were made:—

(1) There is a high incidence in medical students at Lahore of active tuberculosis. 2.2 per cent of students in their first year at the college were found to have positive radiological signs with signs of toxæmia, as shown by a raised sedimentation rate or a slightly raised temperature. Clinical examination without radiography had failed to show the disease, which can only be diagnosed by routine radiography of the chest.

(2) Many of those with positive skiagrams have no clinical symptoms and are unaware that anything is wrong. The majority of these students carried on with their normal work and developed no active disease.

(3) Those students who developed active clinical tuberculosis during their medical training had positive Mantoux reactions on admission to the college and also had radiological

signs of chest disease. This aspect of the work was not completed and this deduction is given tentatively. Obviously more evidence is essential before coming to a final conclusion.

(4) The need in the future for routine radiological examination of all medical students, and of the whole hospital staffs, including nurses, is clear. The high incidence of active tuberculosis in the lower paid servants of hospitals is well known in India.

(5) As this group of Punjab medical students is representative of the class of Punjabis from which army officers are drawn, there is a strong case for miniature mass radiography for army recruits, especially of the officer class from the Punjab. Such a suggestion was made from Lahore in 1941.

(6) Owing to the frequency of tuberculosis in the Punjabis and in Indians generally, a chest skiagram is essential in any suspected case.

The results obtained show a much higher incidence than has been recorded in England and America in similar studies. All whose work is connected with tuberculosis in India are only too familiar with its very high incidence.

The war unfortunately interrupted this work. Studies were incomplete on:—

(1) Early development, progress and significance of radiologically active tuberculosis in Punjabis.



(2) Significance of ++++ Mantoux reactions.

(3) Similar studies in other classes of Punjabis.

(4) The relation of sub-clinical tuberculosis, as shown by a positive Mantoux reaction, to the later development of active disease in Punjabis.

Medical students offer an ideal opportunity for such studies, which I hope to continue after the war.

I wish to thank the British Medical Association, Punjab Branch, and the Indian Research Fund Association, for grants of money, and the medical officers in charge of the X-ray Department, Mayo Hospital, Lahore, Dr. Wig, Dr. Nand Lal and many house physicians for their help.

## A STUDY OF THE INTRADERMAL TEST OF ROTTER FOR VITAMIN C STATUS

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THE intradermal test for the estimation of the level of vitamin C nutrition of the body was suggested by Rotter (1937). He observed that when 0.01 c.cm. of a N/400 solution of the dye 2 : 6-dichlorophenol indophenol was injected intradermally, the colour of the dye disappeared gradually. When methyl blue was similarly injected, its colour remained unchanged, which showed that the decolorization of dichlorophenol indophenol was not due to resorption but to reduction. Rotter (1938) also observed that when the dye was injected into an isolated piece of living skin, or into the skin of limbs separated from the general circulation by a ligature, the skin was decolorized as quickly as in normally living skin. This indicated that the fading of colour was not due to the simple migration of the dye. The time taken for the vanishing of the colour was stated to be dependent on the ascorbic acid content of the skin, and the time was related to the vitamin C status of the body. Rotter's observations were confirmed by Portnoy and Wilkinson (1938), Suzuki (1939), Beck and Krieger (1939), Banerjee and Guha (1939, 1940, 1942), Dolle (1941) and Reddy and Sastry (1941). In the hands of Poncher and Stubenrauch (1938), Jetter (1938), Zoccoli and Lombardo (1938), Goldsmith, Gowe and Ogaard (1939), Poulsen and Lieck (1939), Rapaport and Miller (1939) and Bakhsh, Kochhar and Malik (1940) the intradermal test received no recognition as a reliable index for the assessment of vitamin C nutrition. Wright and MacLenathen (1939) reported that there was a wide variation in the decolorization time in the intradermal test. When two intradermal injections of a solution of 2 : 6-dichlorophenol indophenol were given within a few centimetres of each other on the volar surface of the same forearm, a difference as great as ten minutes in the decolorization

time was observed in one case. When the test was performed in different parts of the body, widely varying results were obtained. Wright and MacLenathen (*loc. cit.*) thus doubted the unreliability of the intradermal test time as an index of vitamin C nutrition of the body.

It was therefore considered necessary to study the variations in the intradermal test time when performed on the same part of the body on different days and also on different parts of the body on the same day. In the present investigation, day to day variation in the intradermal test time, variation when the test was performed on two and four neighbouring spots of the same forearm, and variation when the test was done on two forearms were studied.

Increasing evidence has accumulated to show that vitamin C confers a certain protection from various ailments. This has been well reviewed by Bicknell and Prescott (1942) and Banerjee (1943). A study of the optimum requirement of vitamin C for the body was therefore considered desirable.

The protein, fat, calcium, phosphorus and iron values of the cooked diet as consumed by college students in Calcutta in the three distinct seasons of the year, namely, the winter, the spring and the rainy season, were determined by Banerjee (1941). This investigation revealed that the amount of all the food constituents studied that were consumed by the students varied significantly in different seasons, and the diet was nutritionally poorest in the rainy season. A study of the seasonal variation in the vitamin C nutrition of the body of students was therefore of interest.

The optimum requirements of vitamin C and the seasonal variations in the vitamin C status of the body were, therefore, investigated.

### *Experimental*

#### *(a) Variations in the intradermal test time*

The technique of the intradermal test was that previously described (Banerjee and Guha, 1939). The intradermal test was performed on the volar surface of the forearm of several persons, and the test was repeated on these persons at definite hours of the day on different days. The results are given in table I. In several persons the test was performed on two and four neighbouring spots of the same forearm, and in several others on two different forearms. The results are shown in tables II, III and IV.

#### *(b) Optimum requirement of vitamin C*

Six post-graduate students of the University of Calcutta were fed with 200 mg. of vitamin C daily for a period of three weeks and their intradermal test time and three hours' urinary excretion of ascorbic acid (Harris and Abbasy, 1937) were determined every week. During the period of investigation the students did not receive any extra vitamin C from other sources. The results are given in table V.

(c) Seasonal variations in the vitamin C status of the body

The intradermal test time and 24 hours' urinary excretion of ascorbic acid were determined in five students in the month of February and in ten students in the month of September. The results are given in table VI.

TABLE I

Day to day variation in the intradermal test. The intradermal test was performed on the middle third of the right forearm on its medial aspect

Subject	INTRADERMAL TEST TIME		Day
	Min.	Sec.	
K. R.	6	5	1
	6	40	2
	6	15	3
B. D.	11	0	1
	11	50	2
	7	20	3
	10	45	7
A. M.	8	30	8
	9	0	9
	5	0	1
	5	15	2
	5	15	3
	5	0	6
	4	30	7
	5	15	8
K. S.	5	15	9
	6	30	1
	6	20	2
	6	50	3
	6	45	6
	6	45	7
D. R.	6	35	8
	6	5	9
	12	30	1
	10	30	2
	10	0	3
	9	0	6
G. D.	9	25	7
	9	15	8
	9	5	9
	8	0	1
	9	0	3
	7	45	6
	8	10	7
	9	0	8
	8	30	9

TABLE II

The intradermal tests done on the same individual on two neighbouring spots on the medial aspect of the middle third of the right forearm

Subject	FIRST INJECTION		SECOND INJECTION	
	Min.	Sec.	Min.	Sec.
A. R.	6	15	7	30
S. M.	5	35	6	50
S. C.	7	45	6	20
S. G.	7	0	7	30
J. R.	6	35	6	45
J. S.	5	40	6	0
B. S.	8	0	8	15
F. S.	8	0	7	35
R. B.	8	15	9	0
K. C.	6	0	8	0
K. B.	7	0	7	0

TABLE IV

The intradermal tests done on the same individual on both the arms

Subject	RIGHT FOREARM		LEFT FOREARM	
	Min.	Sec.	Min.	Sec.
D. R.	9	0	10	0
J. D.	13	30	12	30
D. R.	13	30	15	0
U. C.	9	0	8	30
P. R.	8	30	9	0
S. D.	9	15	7	45
A. M.	4	30	6	30
A. C.	4	0	6	30
K. B.	7	0	7	0
R. P.	10	0	11	0
S. S.	11	30	8	30
K. R.	10	0	11	0
S. M.	7	30	8	30
I. B.	11	55	12	0
S. R.	10	15	9	45
A. G.	9	10	8	10
D. G.	9	0	9	30
N. S.	6	0	7	0
K. B.	5	45	6	15
P. G.	11	0	9	45

TABLE III

The intradermal tests done on four neighbouring spots on the medial aspect of the middle third of the left forearm

Subject	FIRST INJECTION		SECOND INJECTION		THIRD INJECTION		FOURTH INJECTION	
	Min.	Sec.	Min.	Sec.	Min.	Sec.	Min.	Sec.
S. R.	7	0	8	0	7	0	8	0
B. G.	7	15	7	12	6	30	7	8
S. S.	6	6	6	22	6	45	5	50
B. S.	6	35	8	0	7	30	8	30
A. S.	5	15	6	15	5	50	6	55
B. D.	6	10	6	15	8	10	8	30

TABLE V

*The intradermal test time and the three hours' urinary excretion of ascorbic acid in individuals receiving a daily dose of 200 mgm. of ascorbic acid*

Subject		0 week	1st week	2nd week	3rd week
R. P.	Intradermal test time ..	5 min. 0 sec.	5 min. 30 sec.	5 min. 30 sec.	5 min. 30 sec.
	Three hours' urinary ascorbic acid	2.57 mg.	4.58 mg.	4.74 mg.	2.64 mg.
P. P.	Intradermal test time ..	8 min. 0 sec.	5 min. 30 sec.	3 min. 45 sec.	2 min. 45 sec.
	Three hours' urinary ascorbic acid	3.37 mg.	21.77 mg.	17.58 mg.	7.0 mg.
B. D.	Intradermal test time ..	12 min. 30 sec.	5 min. 0 sec.	5 min. 0 sec.	5 min. 0 sec.
	Three hours' urinary ascorbic acid	6.07 mg.	4.16 mg.	12.39 mg.	30.79 mg.
K. S.	Intradermal test time ..	8 min. 30 sec.	5 min. 0 sec.	5 min. 0 sec.	4 min. 30 sec.
	Three hours' urinary ascorbic acid	6.07 mg.	4.16 mg.	12.39 mg.	30.79 mg.
S. R.	Intradermal test time ..	10 min.	6 min. 0 sec.	5 min. 0 sec.	5 min. 0 sec.
	Three hours' urinary ascorbic acid	1.64 mg.	17.18 mg.	9.20 mg.	5.65 mg.
N. G.	Intradermal test time ..	8 min. 30 sec.	5 min. 45 sec.	5 min. 45 sec.	5 min. 0 sec.
	Three hours' urinary ascorbic acid	0.96 mg.	14.87 mg.	14.83 mg.	21.99 mg.

TABLE VI

*Seasonal variation in the vitamin C nutrition of the body*

Number	Subject	INTRADERMAL TEST TIME		24 hours' urinary ascorbic acid (mg.)
		Min.	Sec.	
(a) <i>Experiments done in September</i>				
1	D. R.	5	45	40.1
2	D. R.	11	0	9.8
3	G. D.	9	15	13.5
4	S. D.	5	30	15.9
5	R. P.	5	0	20.6
6	P. P.	8	0	27.0
7	B. D.	12	30	4.6
8	K. S.	8	30	48.6
9	S. R.	10	0	13.1
10	N. G.	8	30	7.7
(b) <i>Experiments done in February</i>				
	B. G.	2	10	83.2
	D. R.	2	30	63.4
	J. D.	2	30	105.6
	S. G.	1	50	47.0
	A. G.	2	0	36.8

### Discussion

Tables I to IV show only slight variations in the results of the intradermal test when performed on the same individual on the same day or on different days. Tables II and IV have been statistically analysed to see if the two sets of readings in each table are on the whole different from each other. The mean difference of the readings in each table is found to be . . . . . The variations in the other tables are also equally unsystematic. Hence the test, when applied to a group of individuals, provides a fair index of the average vitamin C status of the group. On the other hand, when applied to a particular individual the test does not provide a strict quantitative measure, but gives a rough estimate of the vitamin C status of the individual.

From table V it is observed that the decolorization time gradually comes down in most of the cases from the original value on the continued daily administration of 200 mgm. of vitamin C. This shows that the body is not saturated with vitamin C at the beginning, and the vitamin is being stored in the system. The minimum decolorization time of 1 minute and 30 seconds, which denotes saturation of the body (Banerjee and Guha, 1940), was not obtained in any of these cases even on the daily administration of 200 mgm. of vitamin C for three weeks. This proves that this dose of ascorbic acid cannot saturate the human body. The physiologically optimum requirement of vitamin C may, however, be less than the amount required to saturate the body. About the relation between the optimum requirement and the saturation dose we have, however, at present little exact knowledge.

In most of the cases in table VI, when the urinary excretion of vitamin C is high, the decolorization time in the intradermal test is low. It is observed that in the month of February (winter) the daily urinary excretion of vitamin C was considerable (36.8 mgm.—105.6 mgm.) but in the month of September (late rainy season) the excretion was low (4.6 mgm.—48.6 mgm.). The corresponding decolorization times in the intradermal test in these two months were respectively 2 minutes 30 seconds to 1 minute 30 seconds and 12 minutes 30 seconds to 5 minutes. This shows strikingly that in the month of February the bodies of these students are more or less saturated with vitamin C, while in the month of September the bodies of students are far from saturation, and in some cases they are deficient in vitamin C. This is obviously related to the greater consumption of fresh vitamin C-rich fruits such as oranges and tomatoes and leafy vegetables, cabbage, etc., which are available in Calcutta in the winter and spring months as compared with the rainy season and early autumn, when such fruits and vegetables become relatively scarce.

## Summary

The variations in the decolorization time in the intradermal test in the same individual on the same day and also from day to day have been measured. These variations are slight and not systematic.

Two hundred milligrammes of ascorbic acid administered orally per day for a period of three weeks to the students under investigation cannot saturate the body if the intradermal test is considered to be the index of vitamin C nutrition. The physiologically optimum dose may, however, be lower than the saturation dose.

There are seasonal variations in the vitamin C nutrition of some of the students. During February the body is nearly saturated with vitamin C. In September, the vitamin C nutrition of the body is much lower, apparently due to the difference in the diet consumed during these different seasons.

The author is indebted to Professor Dr. B. C. Guha, Head of the Department of Applied Chemistry, University of Calcutta, in whose laboratory most of the work was carried out.

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## BACTERIAL STANDARDS FOR ICE-CREAM

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and

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WITHIN the last two or three years, the manufacture and consumption of ice-cream in the city of Calcutta have enormously increased. Numerous small and large cafés and restaurants have sprung up, and most of them are preparing and supplying ice-cream to their customers, civil and military. The production of ice-cream by large scale manufacturing companies has gone up tenfold and more, and the ice-cream is also being widely distributed. Knowing as we do that the raw milk available in Calcutta is mostly of poor quality from the bacteriological point of view, and that milk may often be a potent source of pathogenic micro-organisms, the military authorities raised the following questions: (1) What is the quality of the ice-cream that is being sold? (2) Is the ice-cream safe for the troops and others to eat? (3) What should be the standard prescribed, failing the attainment of which the ice-cream may be prevented from being sold to the troops? To answer these questions we undertook an investigation on the quality of ice-cream sold in Calcutta and consumed by troops in particular. Three reputed makers who were considered 'first class' and three others who were considered 'second class' were selected. Ice-cream from both classes of makers was being eaten by the troops. Several samples from each were collected and examined over a period of eight months. In all, 120 samples were tested and the results are discussed in this communication.

**Technique.**—The samples of ice-cream were collected by army medical inspectors and sent to us preserved in ice. The samples were examined (i) for presence of coliform organisms and (ii) for total number of bacterial organisms. For the coliform test the technique recommended by the Ministry of Health (1940) for water analysis was employed.

After scraping off the surface with a sterile spatula, the required quantity of ice-cream was transferred to a sterile wide-mouthed glass-stoppered bottle under aseptic precautions. It was allowed to melt at room temperature and after a few minutes it was thoroughly mixed by shaking. Various dilutions were prepared, with sterile distilled water. One c.c. quantities of the dilutions and of the undiluted sample were inoculated into MacConkey's bile-salt lactose broth and incubated at 37°C. for 2 days. Three tubes of broth were used for each dilution. The production of acid and gas in the MacConkey's broth was taken as presumptive evidence of the presence of coliform bacilli and the dilution in which coliforms were absent in 2 or more tubes was recorded. For the total count the plate method was used. The number of colonies present were counted after incubation for 2 days at 37°C. The number of organisms in 1 c.c. was calculated and recorded.

**Results.**—Of the 120 samples from 6 different sources examined the results were as follows:—

*'Coliform' test.*

Result	Number of samples
Absent in 1 c.c.	49
" " 0.1 c.c.	27
" " 0.01 c.c.	21
" " 0.001 c.c.	9
" " 0.0001 c.c.	11
" " 0.00001 c.c.	3
	<hr/> 120

The best sample from the 'first class' makers gave nil in 10 c.cm. and the worst sample gave nil in 0.00001 c.cm. The best sample from the 'second class' makers gave nil in 0.01 c.cm. and the worst gave nil in 0.00001 c.cm.

*Total colony count*

Result	Number of samples
100 or below	2
1,000 " "	40
10,000 " "	44
50,000 " "	11
100,000 " "	5
200,000 " "	7
500,000 " "	4
Over 500,000	7
	<hr/> 120

The best sample from the 'first class' makers gave a count below 100 per c.cm. and the worst gave below 500,000 per c.cm. The best sample from the 'second class' makers gave a count below 10,000 per c.cm. and the worst gave over 500,000 per c.cm.

**Discussion.**—In the U.S.A. most states are adopting a standard of 100,000 bacteria per c.cm. Reports of examinations however show that in most samples tested the counts were below 25,000 per c.cm. and in the better class ones the counts gave less than 10,000 per c.cm. The non-inclusion of the test for coliform organisms in the final standard for ice-cream in most states in America does not imply that these states do not attach any special importance to coliform organisms, but merely that because of the insistence on certain preliminary standards, such as the quality of milk used, method of pasteurization and so on, they feel certain that the coliform organisms would have been eliminated by the preliminary treatment. The fact that a few cities and one state in the U.S.A. are insisting on the absence of coliform organisms in ice-cream (Fabian, 1937) shows that this is considered important, and the possibility of contamination after pasteurization is kept in view. In fact the book on standard methods for examination of dairy products published by the American Public Health Association (1939) says that 'coliform organisms should be absent from the mix after pasteurization and, if need be, the temperature of pasteurization should be adequately raised to ensure this'.

In England, Bardsley (1938), after examining 237 samples in Manchester, recommends the

following standards as regards coliforms and total count. 'Standard A': (i) No coliform organisms in less than 0.1 c.cm. (ii) Total counts of not more than 200,000 organisms per c.cm. on Yeastrel milk agar after 2 days' incubation at 37°C. 'Standard B': (i) No coliform organisms in less than 0.01 c.cm. (ii) Total counts of not more than 500,000 organisms per c.cm. on Yeastrel milk agar after 2 days' incubation at 37°C.

From a perusal of the results obtained by us, it will be seen that; judged by the total count, 85 per cent of samples satisfy the U.S.A. standard and 90 per cent satisfy Bardsley's class 'A'. But if the samples are judged by the coliform count, about 40 per cent conform to American standard and 63 per cent to Bardsley's class 'A'. Here it should be pointed out that the earlier samples were less satisfactory than the later samples. The repeated visits by the army medical inspectors and the improvements in manufacture that they brought about were probably responsible for the better quality of the later samples. Therefore it would appear that the following standards would be suitable for India:—

Class 'A'.—No coliform in less than 0.1 c.cm. Total count less than 100,000 per c.cm.

Class 'B'.—No coliform in less than 0.01 c.cm. Total count less than 200,000 per c.cm.

In our class 'A' we have taken Bardsley's class 'A' coliform standard and the American standard for total count and in our class 'B' we have accepted Bardsley's class 'B' coliform standard and her class 'A' total count.

Judged by this tentative standard, of the 120 samples examined 73 or 61 per cent fell under class 'A'; 21 or 17.5 per cent fell into class 'B' and 26 or 21.5 per cent fell below class 'B'. Had we examined samples from third class cafés or small scale manufacturers, we have no doubt that the quality would have been very unsatisfactory.

**Conclusion.**—Bacterial standards for ice-cream sold in India are suggested. Since in India intestinal infections are widely prevalent, insistence on such a standard for ice-cream, which is being increasingly consumed, is highly desirable.

Although we have suggested tentatively the above standards, we are really in favour of adopting a more rigorous standard for coliforms than the one suggested. Our examination of samples taken at different stages of preparation of ice-cream has revealed that coliform organisms are mostly being introduced at stages subsequent to pasteurization and, as in some cases these organisms were of the faecal type, we feel that as low a coliform count as possible should be insisted upon in order to minimize the risks of contamination with intestinal pathogens.

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[Note.—Some time ago the standards of ice-cream in Calcutta were investigated by the army authorities and were, it is believed, found highly unsatisfactory. Steps were made to improve things, and the findings above reported were made after these steps had been taken. It is hoped that the manufacturers will attempt to maintain and improve the present standards and not relapse into the condition which was found previously.—EDITOR, *I. M. G.*]

## A Mirror of Hospital Practice

### A CASE OF MYASTHENIA GRAVIS

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MYASTHENIA GRAVIS has been defined as a syndrome in which there is undue fatigue of the muscles. It may later on be followed by a permanent weakness which may simulate paralysis of the muscles. Erb gave the name of myasthenia gravis in 1879. Wills described it in 1887.

The usual age incidence is between 15 and 50 years. More commonly it occurs between 15 and 30 years. Females are affected more than the males. It has a familial tendency. More than one member of a family has been known to suffer from this disease.

The onset is usually insidious. The patient begins to notice fatigue of the muscles coming on towards the end of the day, after the day's work, while he is comfortable in the morning after resting at night. The disease is precipitated by any infectious condition, *e.g.*, influenza, pneumonia and encephalitis lethargica, etc., or even by pregnancy or labour.

Any muscle of the body may be affected. In some cases all the muscles may suffer. The disease usually starts in the muscles supplied by the cranial nerves, though other muscles of the body may be the first to be picked out. The involvement of the ocular muscles gives rise to ptosis on one side or both. This is due to the affection of the levator muscles of the upper eyelids. Diplopia may also result from fatigue of the external ocular muscles, and this may be marked towards the evening, whereas it disappears next morning after resting at night. Pupillary reflexes may be normal or sluggish. Difficulty in chewing may arise from weakness of the muscles of mastication, and this may be more pronounced

towards the later part of the meal, while the initial act of chewing might have been quite normal. Swallowing may be affected when the muscles of deglutition are involved; even regurgitation through the nose may occur. Articulation may be affected due to the involvement of the soft palate, laryngeal muscles, etc., or hoarseness of voice may result. When the facial muscles are affected, weakness of the orbicularis oculi may prevent the patient from closing his eyes properly, and weakness of the orbicularis oris may prevent him from laughing and whistling. The involvement of the muscles of the arms causes difficulty in raising the upper limbs, or difficulty in working may arise. Involvement of the lower limb muscles makes the patient's walking difficult. When the neck muscles are affected, they cannot support the head for long. The involvement of the diaphragm and the intercostal muscles interferes with proper respiration, and in some cases may give rise to severe dyspnoea. Disturbances of micturition and defaecation have also been reported.

On clinical examination of the muscles, the tone is found to be lost. There is no wasting in the beginning, but when the disease has lasted for a long time, atrophy may occur. Reaction of degeneration is never found. Fibrillary twitches are not usually seen, though they may occur. Sensory changes are not found, and reflexes are normal. Blood examination shows some leucocytosis. The blood chemistry has not been worked out, but calcium metabolism shows some impairment. It is usually diminished. There is also diminished sugar tolerance, the glucose content of the muscle is increased, and the urine may contain creatinine.

In 1891, the electrical reaction which occurs in the muscles and is rather characteristic of the disease was described by Jolly—the myasthenic reaction. When the muscle is subjected to faradic stimuli, it gradually loses the power to respond to it, but it retains its contraction to galvanism. Some time after the response to faradic stimuli has been lost, a re-test shows that the faradic stimuli cause contractions again. This may also happen after an injection of prostigmine.

The course of the disease is rather slow, but in some cases may progress rapidly and may end fatally in one to three years. Remissions in the disease have been noticed in repeated pregnancies.

Regarding the pathology of the condition, the observations have not been constant. Some have found degenerative changes in the spinal cord, and small hæmorrhages in the nuclei of the ocular, facial and the hypoglossal nerves. The muscles which are involved are œdematous and swollen, infiltrated with lymphoid cells (lymphorrhages). There are collections of cells lying between the muscles, and sometimes within the muscle fibres. There may be some muscular atrophy. The thymus has been found to be en-



larged in 50 per cent of the cases. Lymphorrhages are also found in them and also in the thyroid, liver, suprarenals, kidneys, lungs, heart and pancreas.

The modern conception of the disease is that there is defect in the conduction of the impulses from the nerve endings to the muscle fibres, that is, a defect at the myoneural junctions. Acetylcholine is necessary for such conduction at the myoneural junctions. In myasthenia gravis this is destroyed, or its production is inhibited by an enzyme called cholinesterase. This conception regards its causation as a chemical one. No structural lesion has been reported in this disease. One thing worthy of note is that blood examinations have never shown any increase of the cholinesterase in patients suffering from myasthenia gravis.

#### *Treatment*

The patients should have absolute rest, which has to be prolonged. There is a tendency for these patients to feel much depression and discouragement, and therefore it should be the duty of the physician to give them encouragement in order to relieve their mental distress.

The diet should be easily assimilable and rich in vitamins. When mastication cannot be performed satisfactorily, semisolid diets—fruits and vegetables should be given thoroughly grated, or liquid diet may be prescribed. In some cases when swallowing is troublesome, resort may be had to artificial feeding.

The drug treatment of the disease has not been satisfactory. Those which have been used are: ephedrine tablets gr.  $\frac{1}{2}$ , glycine 10 gm. daily, acetylcholine, physostigmine salicylate gr. 1/100, strychnine, atropine gr. 1/150 and prostigmine. No clinical improvement has resulted after the use of glycine, acetylcholine, parathormone, strychnine and atropine. Ephedrine helps the patient to a certain extent and so also does physostigmine salicylate. Prostigmine is a drug of choice. It is closely related to physostigmine in its chemical structure and action. The dose is 0.5 to 2 mgm. in tablets, daily. More than this may be given if needed. Larger doses when given are better administered along with atropine gr. 1/200 to counteract the excessive peristalsis. It may also be given by injection hypodermically or intramuscularly 1 c.cm. containing 0.5 mgm. or concentrated solution 1 c.cm. containing 2.5 mgm.

Alcohol makes the condition of the patient worse, and should therefore be avoided. Quinine also worsens their condition, and myasthenic patients may become worse when it is administered if they happen to contract malarial infection. This should be borne in mind in the management of these cases. Massage of the body is best avoided because it increases the fatigue. In cases in which the Wassermann reaction of the blood is positive, it might be worth while trying antisyphilitic treatment along with prostigmine.

#### *A case report*

A Hindu male, aged 50 years, a farmer by profession, was admitted into the Thomason Hospital, Agra, on 11th February, 1943, with the following history:—

Four months before, he noticed gradual weakness of the whole body which used to become marked about midday (being a farmer by profession he had to work hard in the morning). On rising in the morning, he felt well, but the weakness increased till it was at its worse in the afternoon. This weakness he first noticed in both the upper extremities while he was taking a bath. Then he noticed weakness in the lower extremities. He felt difficulty in getting up from the sitting position. When he squatted for micturition or defecation, he felt difficulty in getting up in the beginning; later he could not get up immediately after the act. But after resting for a while, he got up easily and the weakness was also not so marked. Later he felt weakness in the fingers and could not hold things tightly.

At the same time he noticed weakness in both the upper eyelids, first in the left and then in the right eye. The weakness increased and for the past six weeks he had been unable to open the eyes properly.

About two months before admission he felt some difficulty in mastication, and a few days later he could not masticate at all, and had to remain on liquids only. When he was in the hospital, he felt difficulty in swallowing, and sometimes this difficulty was so great that regurgitation of fluids occurred through the nose and nasal feeds were used. He could not laugh properly and could not whistle. When asked to take a deep breath, he could not do so, though when screen examination was done he did not show any impairment of diaphragmatic movements. He could not lift the arms more than 45° in the sitting position, but while lying flat in bed he could raise both the arms up to 90°. When his legs were extended, he could not flex them. He used to flex them with the help of his hands. He became easily tired while sitting up for a long time. He could not keep his neck erect in this position for long and had to exert himself to keep his neck erect.

When he talked for some time, he felt difficulty in speaking. There was drooping of the eyelids and while walking he had to tilt his head a little forwards. The pupillary reaction was a little sluggish but the vision was unimpaired. The jerks were also sluggish and the muscles were somewhat wasted. No abnormality was detected in the respiratory, circulatory, gastro-intestinal, nervous and genito-urinary systems. Pathological and biochemical investigations of blood revealed no appreciable abnormality.

While he was in the hospital he had been always constipated, and aperients and enemas had to be given freely. Sometimes these measures did not succeed, and at one time he remained constipated for seven days. The ptosis of the eyes was very pronounced. The ophthalmologist was consulted and he reported 'External ophthalmoplegia with myasthenia gravis: ptosis. Fundus normal'.

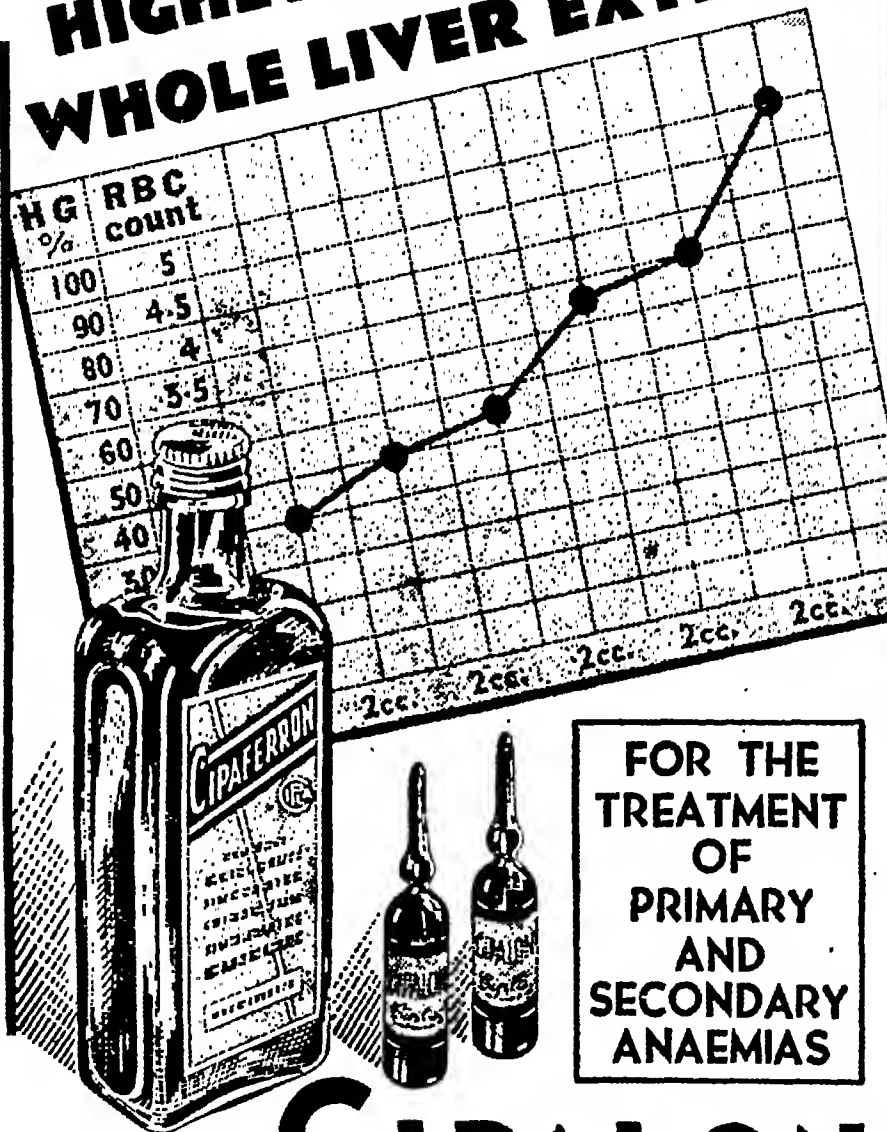
The drugs used were physostigmine salicylate, gr. 1/100 by injection and ephedrine gr.  $\frac{1}{2}$ . They relieved the patient of the muscular fatigue only temporarily for 6 to 8 hours. Prostigmine was not used, being not available. He left the hospital on 11th April.

I wish to thank Major-General H. C. Buckley, I.M.S., Superintendent of the Hospital, for allowing me to publish the case.

#### **SPECIAL TUBERCULOSIS NUMBER**

For several years the October issue has taken the form of a special tuberculosis number. This year owing to the late receipt of manuscripts from the Tuberculosis Association of India this has not been possible. It is hoped to publish a special tuberculosis number at a later date. This will be announced at least a month beforehand.

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# Indian Medical Gazette

SEPTEMBER

## PARA-SPRUE

ELSEWHERE in this issue we publish an article in which Dr. A. Bramwell Cook describes a deficiency state of which the salient features are diarrhoea, glossitis and anaemia with pigmentation of the skin. The patient's appetite is impaired, he suffers from flatulent dyspepsia and abdominal discomfort, and exhaustion and weakness are prominent. The syndrome reminds one of sprue, but the copious pale, fermenting and porridgy stools with high fat content are seldom seen, and instead they are more often watery and contain undigested food. It is of relatively common occurrence in this country, especially among the victims of chronic colitis or some other chronic gastro-intestinal disorder, who subsist on very low ill-balanced diet, deficient in proteins and vitamins. It occurs not only among the poor Indians but also in better-class people, including Europeans and Anglo-Indians, who as a result of bowel disturbances are kept on a restricted diet for a long time. Dr. Cook has seen several cases in the same family, and this observation suggests the view that the disease is basically dietetic. Chronic dysentery, malaria and pregnancy are important predisposing factors. The *sutika* of Indian women during the puerperium affords a good example of it. Surprisingly little is known about the essential pathological changes in this condition. Of the biochemical changes the glucose-tolerance curve is usually low or normal, but occasionally there is a flat curve indicating failure of intestinal absorption. The gastric secretion usually contains free hydrochloric acid. Sometimes there is slight increase of split fat in the faeces apparently due to intestinal hurry; but it is seldom over 30 per cent of the weight of dried faeces as is usually the case in true sprue.

Vitamin B<sub>1</sub> has for long been known to influence the normal physiological activity of the gastro-intestinal tract, and more recently other members of the vitamin B complex have been implicated as essential for normal digestive activity. Mackie in 1933 observed certain changes in the small intestine in association with certain nutritional disorders such as tropical sprue, celiac disease, idiopathic steatorrhoea,

etc., and these observations, much of which are the result of radiological studies, have been confirmed by various other writers. In mild disorder of intestinal function, motility and tonicity are increased but later diminished. There is often alteration in the outline of the mucosal folds, the normal feathery or herring-bone appearance being lost, and abnormal segmentation may occur. These radiological changes are commonly referred to as the 'deficiency pattern' of the small intestine. Such deficiency has been produced in dogs on a diet lacking in vitamin B, and therapeutic tests have supported the view that one or more components of the vitamin B group are associated with its development. The mechanism responsible for this functional disability of the small intestine is still a matter for discussion.

The syndrome under discussion is usually regarded as a state of malnutrition, the primary defect being faulty absorption from the intestine. Dr. Cook suggests that this syndrome is a variant of sprue, the nature of the stool being conditioned either by the predominantly carbohydrate nature of the diet or by some particular deficiency of the vitamin B complex. This deficiency may be primary, due to its lack in diet, or it may be secondary, due to its poor absorption resulting from disease of the small intestine. Thus bowel changes may be the result of the deficiency or might be its cause. But there is another side of the story; the radiological changes are not in themselves specific for vitamin deficiency. They may result from other conditions, the most important being diseases associated with hypoproteinaemia such as nephrosis and diseases of the liver. On the other hand a vitamin deficiency may exist without disturbance of the small intestine. It is obvious that the causative factors can be determined only by further clinical studies.

The syndrome described is not classical sprue, pellagra, beri-beri or ariboflavinosis. It is a distinct clinical entity characterized by chronic watery diarrhoea with nutritional macrocytic anaemia, although certain signs such as wasting and glossitis are suggestive of sprue. In fact, these cases in Indians are frequently diagnosed as sprue. Sometimes the condition is regarded as a forerunner of sprue, and is referred to as 'pre-sprue' because it has features in common with true sprue, and some cases of sprue start in this way. But if the name is meant to imply that all cases of sprue commence this way, or that all cases of this condition progress to become sprue if untreated, then it is a misnomer. A patient may suffer from this condition for a long time and may even die of it without passing into sprue stage. The word 'para-sprue' would be a better name, and in this number the readers will also find an account of 22 such cases by Chaudhuri and Rai Chaudhuri in which the clinical and biochemical findings tend to show the condition as a distinct clinical entity although a very small proportion may have

features indistinguishable from those of true sprue. These cases responded well to parenteral administration of crude liver extracts and good diet. Perhaps the most remarkable feature of these results was that they were achieved without the tedious dietetic restrictions that are essential in the management of true sprue.

R. N. C.

## ANIMAL SERA FOR TRANSFUSION PURPOSES

UNTIL a few years ago, whole blood was the usual transfusion fluid. Later it became clear that, for some conditions, blood plasma or blood serum was as good as, or better than, whole blood, and moreover they were much more easy to store. Later on it was found that blood plasma or serum could be dried and stored in powder form for an almost indefinite period, and could be rapidly reconstituted and used for transfusion purposes.

Blood banks which were originally started to provide whole blood have developed along the lines of provision of blood serum or blood plasma either stored or reconstituted after drying.

In normal times it should be possible to meet the limited need for transfusion fluid from human material, but at the present time with widespread destruction and casualties caused directly by war, and widespread famine and food shortage caused indirectly by war, the demand for blood transfusion work has greatly increased, and in many countries it has been difficult or impossible to meet this demand entirely from human sources.

From time to time, especially during recent years, attempts have been made to use transfusions of animal serum in the treatment of those conditions not necessitating whole blood transfusions. Crude animal serum has been found unsuitable because of the immediate reaction produced and because of the later development of serum sickness in a high proportion of cases. Recently work has been done in attempting to make animal serum suitable for administration to human beings. This work has been mainly along two lines.

Firstly, since the antibodies are known to be attached to the globulin, attempts have been made to remove the globulin fraction leaving a solution of albumin which could be suitable for injection. A certain amount of progress appears to have been made along these lines.

A second line of work has been the destruction of antibodies by controlled heating so that the resulting product was tolerated by man. Edwards has published three papers, two in 1943 and one in January 1944, describing the

results of this work. He has found it possible by the treatment of bovine serum with formalin and ammonia and heating to 73°C. to destroy the antibodies present in the serum and to make the bovine serum suitable for administration to man. [The most recent article is abstracted in our present issue (page 447).] The serum resulting from this treatment Edwards calls Despeciated bovine serum; D.B.S. The physical properties are found to be similar to those of human plasma. It has been found that D.B.S. can be safely kept at room temperature for several months. Edwards reports preliminary clinical trials of D.B.S. in 26 cases. Ordinarily 400 c.cm. have been transfused into patients within one hour, but up to 2,400 c.cm. have been given within 20 hours; in two cases of shock, 1,200 c.cm. have been given within 45 minutes. In two of the 26 patients, the temperature rose to 100°F.; in one of the 26 patients, vomiting was seen; this was in a patient who had received 1,200 c.cm. in 45 minutes. In the remaining 23 cases, reaction was completely absent. Serum sickness and delayed reaction also were absent. The fluid and its contents appeared to be retained in the circulation, and the osmotic pressure effects appeared to be considerable.

This work appears to be of great interest. In the first place, despeciated bovine serum can be prepared very easily and in large quantity, and can be stored indefinitely. In the second place, the need for some such transfusion material appears to be rapidly increasing. In the Bengal famine for example, in the treatment of acute inanition, supplies of such serum might have been invaluable. In dealing with starvation and famine in war devastated areas, it appears that such a transfusion fluid might be of inestimable value.

Here in India, blood banks are having considerable difficulty in providing adequate supplies of transfusion material from human sources. The introduction of suitable animal serum for suitable cases might greatly relieve the pressure on the blood banks. The available sources of animal serum are infinitely greater than the available sources of human transfusion material. From 16 to 20 pints of blood can be collected from an animal slaughtered at a slaughter house.

It is not clear whether sentiment would deprecate the use of bovine serum in this country; if there is a sentimental objection to bovine serum, sheep's serum would probably be equally suitable. It has not been used in England because it is not so readily available in such large quantity.

In the School of Tropical Medicine, Calcutta, and in the All-India Institute of Hygiene, Calcutta, some preliminary work on this subject has been undertaken, and future developments will be watched with interest.

## Special Article

### A VITAMIN B DEFICIENCY SYNDROME ALLIED TO SPRUE\*

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EVERY practitioner in Gujerat frequently meets patients suffering from a triad of symptoms, diarrhoea, glossitis, and anæmia. In one year I have seen over 200 cases, clinical details of 50 which I have kept for analysis. Hardly a day passes without seeing a typical case. The indigenous practitioner recognizes such cases as 'sprue'. The relative frequency of this disease, if it is really sprue, conflicts with the idea commonly quoted in standard textbooks, e.g. Manson-Bahr in 'Manson's Tropical Diseases', 11th edition. 'Sprue is a disease which pre-eminently affects Europeans. Doubt was formerly expressed as to the existence of sprue in native races'. Hamilton Fairley in 'The British Encyclopædia of Medical Practice' writes that 'the disease is very rare amongst Indians'. These statements are true or not according to whether the syndrome I am elaborating is really sprue or not. There is no doubt as to the frequency of this syndrome, but there is doubt in my mind as to whether it is classical sprue or a vitamin B deficiency syndrome allied to sprue.

The salient features are :—

(a) Diarrhoea, the motions being watery and copious and in colour white or yellow. They may be passed at any time of the day, especially after meals and be accompanied by exhaustion.

(b) Glossitis, the tongue is inflamed. It is usually clean and may be red in spots or be glazed in appearance. The patient complains of soreness of the mouth and of inability to eat spices. The glossitis may precede the diarrhoea or occur simultaneously with it or follow it.

(c) Anæmia is usually marked and is frequently macrocytic. In many cases however the anæmia is microcytic.

(d) Pigmentation of the skin. The knuckles of the fingers are black and the face is sallow.

The critical difference from sprue as classically described in textbooks is in the nature of the motions.

Hamilton Fairley in 'The British Encyclopædia of Medical Practice' describes the stools of sprue as being 'bulky and loose in consistence, pale, or occasionally even white in colour and gaseous. Exceptionally during acute exacerbations, an enteric type of diarrhoea may develop with frequent, brownish, fluid stools'. Manson-Bahr in 'Manson's Tropical Diseases' describes the diarrhoea as of two kinds, 'One chronic and habitual, the other more acute and in the early stages,

evanescent. The former is characterized by one or more daily discharges of a copious, pale, greyish, pasty fermenting, acid, mawkish, evil smelling material; the latter is of a watery character, also pale and fermenting, the dejecta containing undigested food, and as a rule, an abnormally large amount of oil and fatty acids'.

The loose type of diarrhoea in sprue is thus described by two authorities as being 'exceptional' and 'evanescent'. In the syndrome I am reviewing, however, the loose, watery diarrhoea is the characteristic, habitual feature. The porridge-like, bulky, frothy stool of classical sprue is seldom met with.

This difference in the nature of the diarrhoea constitutes an essential variant from classical sprue, and justifies the isolation of the disease as a syndrome allied to sprue.

Tropical sprue, non-tropical sprue, idiopathic steatorrhoea and celiac disease are classified together as the 'sprue syndrome'. In the same way this variant of sprue may be accepted as a member of the group of conditions known as 'the sprue syndrome'. Apart from the nature of the diarrhoea, the syndrome is similar to sprue as classically described.

The recent researches into the part played by the vitamin B complex in the physiology of the small bowel, the well-known deficiency of vitamin B in the diet of Indians, and the successful treatment of the syndrome by the administration of vitamin B complex, lead one to the conclusion that the syndrome is due to vitamin B deficiency.

For more than 20 years, it has been known that deficiency of vitamin B is associated with abnormal gastro-intestinal function. Radiological researches in more recent years seem to give the clue to the mechanism of this association. The work began with observation on the small intestine in cases of sprue (Pillai and Murthi, 1931; Mackie, 1933). In these and later studies, mainly by American workers, it was found that characteristic changes occurred in the small intestine in several diseases such as sprue, celiac disease and idiopathic steatorrhoea. The *valvula conniventes* of the duodenum and jejunum normally present a feathery or herring-bone appearance. This appearance is absent in these diseases, and the opaque material separates into smooth, outlined masses of various lengths. These radiological changes are now referred to as the 'deficiency pattern' of the small intestine.

There is growing evidence that one or more components of the vitamin B complex is associated with the development of this 'deficiency pattern'. The deficiency has been produced in dogs on a diet lacking vitamin B, and was only completely cured by the administration of the whole complex (Crandall *et al.*, 1939). Martin and his colleagues (1941) experimenting on dogs found that inositol increased peristalsis in both stomach and small intestine, whereas nicotinic acid decreased peristalsis and induced a state of repose. The authors suggest that the balance of these two factors might determine the motility of the gastro-intestinal tract.

Therapeutic tests also support the theory that the vitamin B complex is probably responsible for the deficiency pattern. Lepore and Golden (1941) describe a series of patients in whom the deficiency pattern was demonstrated and who complained of a series of symptoms which they claim form a clean-out syndrome due to deficiency of the vitamin B complex. The oral administration of yeast or the parenteral injection of liver extract relieved the symptoms, and the deficiency pattern disappeared.

\* Being a paper read at the All-India Medical Conference held at Ahmedabad, December 1943.



The deficiency pattern is due to the flattening out or disappearance of the *valvula conniventes* as a result of paralysis of the main layer of the *muscularis mucosæ*.

This paralysis of the *muscularis mucosæ* leads to loss of pumping action of the villi into the larger lacteals (Hurst). Fat would thus cease to be absorbed, and the stools would thus contain a great excess of split fat, as in sprue. Such a paralysis would not alter the microscopic appearance of the mucous membrane. If the activity of the *muscularis mucosæ* is regained, the mucous membrane being unimpaired, the villi would start to function again and so normal fat absorption would be resumed.

The cause of this paralysis of the *muscularis mucosa*, if this is the correct explanation of the sprue syndrome, may be vitamin deficiency.

This disturbance of the normal physiological activity of the small intestine, presumably due to vitamin B deficiency, results in a corresponding functional disturbance.

Bennett and Hardwick (1940) have coined the term 'chronic jejuno-ileal insufficiency' to denote the resulting syndrome. The symptoms are gaseous, generalized abdominal distension after meals, borborygmi and gas pains in the area of the small intestine, constipation or diarrhoea with loose stools. The biochemical features are achlorhydria or hypochlorhydria, a flattened glucose tolerance curve due to failure of carbohydrate absorption, faulty absorption of fat with increased fatty acids and calcium soaps in the stools, calcium deficiency due to mal-absorption or retention of calcium in the intestinal tract as calcium salts, failure of absorption of iron and of the anti-anæmic principle, resulting in anæmia. Thus is compounded a syndrome of clinical and biochemical features which gives a complete picture of sprue. Stannus (1942) advances a new hypothesis to explain the defect in intestinal absorption. He believes that the physiological lesion in sprue is failure of phosphorylation, an essential process for the absorption of fatty acid glycerol, cholesterol and glucose by the intestinal mucosa. He suggests that this failure of phosphorylation is due to a defect in the enzyme system which is made up of members of the vitamin B. complex, including riboflavin, nicotinic acid, pyroxidine and choline.

The name 'jejuno-ileal insufficiency' places the emphasis on the small bowel and not on the colon. Sprue may be preceded by an attack of amoebiasis which attacks the large bowel essentially—but the symptoms of sprue do not supervene until, due to vitamin B deficiency, as a result of dietetic restriction or failure of absorption, the syndrome of 'jejuno-ileal insufficiency' is produced. Colitis itself does not lead to the clinical and biochemical picture of sprue. In amoebiasis, there may be some secondary anæmia, but never a megalocytic anæmia. The glossitis, achlorhydria, flat glucose tolerance curve, and low serum calcium seen in sprue are not to be found in colitis; they arise when the pathology shifts to the jejuno-ileum.

The evidence that vitamin B deficiency lies at the root of this jejuno-ileal insufficiency is at present practically wholly therapeutic. Lepore and Golden (1941), Mackie (1933), May *et al.* (1942), Manson-Bahr (1941), etc., have shown the remarkable response clinically to an intensive course of vitamin B complex given orally and parenterally. The symptoms disappear, the deficiency pattern radiologically returns to normal, weight is gained. Some experimental work on dogs (Martin and his colleagues) also lends proof to the theory that vitamin B deficiency is responsible for the deficiency pattern. Circumstantial evidence for the theory that vitamin B deficiency is the cause of the sprue syndrome is gained by studying Indian diets. 'The richest sources of vitamin B<sub>1</sub> are unmilled cereals, pulses and nuts. A diet largely composed of raw milled rice contains insufficient vitamin B<sub>1</sub>. The greatest danger of vitamin B<sub>1</sub> deficiency arises when a highly milled raw rice is consumed as the main ingredient in a diet containing other foods, such as

pulses, in very small quantities. There is good evidence that poor Indian diets, which contain little milk or meat, are often very deficient in vitamin B<sub>1</sub> group' (Aykroyd). The deficiency in the vitamin B complex may be relative and not absolute. Sydenstricker (1941) has shown that on a diet consisting largely of carbohydrate, acute riboflavin and nicotinic acid deficiency is apt to occur. Thiamin, nicotinic acid and riboflavin are concerned with the continuous processes of cellular nutrition and respiration. They are essential for the metabolism of carbohydrates. On a diet with a preponderance of carbohydrate, a correspondingly large 'cover' of vitamin B complex is essential. If this is lacking, then symptoms of deficiency may arise. Moore (1939) commented on the 'sore tongue syndrome' on a staple diet of rice.

Experience confirms the above observations. In any particular case, it is difficult to elicit evidence of any gross deficiency in the diet apart from the general deficiency common to all Indian diets. On being questioned, a patient usually replies, 'I eat rice, dhal, wheat and vegetables'. It is not uncommon however to meet with patients who eat only rice and do not eat bajri or vegetables—or others who have dieted themselves for a long period on butter-milk and pulse water only. In such cases there is a manifest deficiency of the vitamin B complex.

Another observation that lends force to the argument that a dietetic deficiency is the cause of the syndrome is that several cases may be met within one family. A husband and wife may be similarly affected. I have met a family in whom the mother and the three children all had glossitis. In another family, the son at first presented himself with the syndrome in all its features. After some time, when he was showing steady improvement, the father asked that he might take his son's bed as he was not well. He had glossitis, anæmia and weakness, but constipation instead of diarrhoea as in the son's case. Turning to the mother, I found she had also glossitis and anæmia. Probably in the father's case, nicotinic acid deficiency was less marked than deficiency of the other elements of the vitamin B complex, and so he did not have diarrhoea.

I consider this disease is the most serious nutritional defect in Gujerat. I speak as a clinician and not as a nutritional research worker. But I recognize this deficiency disease so frequently and see its debilitating effects in so many of my patients that I know of no other avitaminosis which is responsible for as much ill health in the community.

#### CLINICAL FEATURES

##### *Diarrhoea*

(a) *Nature of stools.*—The stools are watery and are often described by the patient as looking like curds and consisting of undigested food. The colour may be yellow or white or greenish. The thick, frothy, bulky, pasty, pale stool of sprue is only occasionally seen.

(b) *Time of day.*—The motion may be passed at any time of the day but not particularly in

the early morning as in sprue. A few patients however specify the night and early morning as the time when the diarrhoea occurs, but most patients, on being questioned, say the stools are passed at any time.

(c) *Lienteric diarrhoea*.—A very characteristic feature is that there is an urgent desire to defæcate after taking food. There may be a motion every time the patient takes food.

(d) *Exhaustion* is felt after passage of the stool.

(e) *Quantity*.—The stool may be profuse and exceed in quantity any food intake of the patient.

(f) *Number*.—The number of motions may vary from 2 or 3 to 10 or 15 in the day.

(g) *Mucus or even blood* may appear in the motion at times. This is not due to chronic dysentery, but due to an acute exacerbation of the disease in which the rectal mucous membrane is injected and inflamed due to the frequent passage of motions.

(h) *Gurgling* and sometimes colic accompany the passage of motions.

*Constipation* may alternate with diarrhoea. One may see a patient who complains of constipation and all the other symptoms suggestive of this syndrome, but in whom diarrhoea had occurred at the onset and only at irregular intervals since.

*Pigmentation*.—A characteristic feature is a dark or even black pigmentation of the knuckles of the fingers. It seems to be an increase of the natural pigment of the skin overlying the joints, and not a rash on the skin as in pellagra. This blackness of the knuckles is very commonly seen, but it is not invariable. Typical cases may be seen with a normal appearance of the skin.

*The common sites of pigmentation* are: on the knuckles, the tongue (black spots may appear on the dorsum of the tongue), around the lips and in the nasolabial folds, on the forehead, under the eyes, on the dorsum of the ankles, back of the wrist, extensor surface of the arms, front of the neck, front of the legs below the knees.

The effect is a characteristic sallowness or murkiness of the complexion. The sallow face with the muddy skin and the sunken cheeks at once suggests the probable diagnosis.

*Glossitis*.—In marked cases, the tongue is clean, smooth, glazed and red. The whole dorsum of the tongue may be red, or the tip only or spots at the sides of the tongue may be red. The redness may extend to the palate and pharynx, and in extreme cases, the whole oropharynx may be inflamed so that the patient has marked dysphagia. Aphthæ of the lower lip frequently occur. When the disease is not so pronounced, the tongue however may not be red and may not even be clean. The tongue may be red and clean during relapses only, regaining its normal colour and even a fur in a remission.

In a series of 50 cases, the tongue was described as:—

Clean and glazed ..	6
Clean and fiery red all over ..	4
Clean and red at tips or sides ..	20
Slightly furred ..	3
Clean but normal ..	17

Angular stomatitis due to riboflavin deficiency was noticed in 3 cases.

The time relationship between the glossitis and the onset of diarrhoea was noted in each case.

Diarrhoea occurred first in 20 cases; glossitis occurred first in 25 cases; the glossitis and diarrhoea commenced simultaneously in 5 cases.

A frequent observation was that the patient had suffered from glossitis on and off for many years, in one case 15 years, before the onset of diarrhoea. One patient said she had suffered from sore tongue since childhood.

Even in cases where there is no gross change in the appearance of the tongue, the patient complains that he cannot eat chillies or hot food.

*Dyspepsia*.—The patient complains that he is unable to take any food. The prominent features are:—

Gurgling in the abdomen. An urgent desire to defæcate after food, loss of appetite (at times there is excessive appetite but the patient is unable to eat because of the stomatitis), vomiting, a feeling of weight and distension after food, heartburn, pain in the epigastrium and occasional colic is complained of.

*Constitutional effects*.—Loss of weight is marked in all cases; exhaustion and weakness are prominent; lack of mental power, inability to concentrate, incapacity to work, and mental depression are seen, and irritability of mind is often noted.

*Paræsthesia*, probably due to thiamin deficiency, is frequently complained of, especially tingling and burning in the legs, soles of the feet, and the palms of the hands. There may be loss of knee jerks. I have observed ataxia in one case.

*Fever* of a low degree 99 to 100 may often be observed. The temperature may persist for some time, as long as the patient is weak, and automatically disappear as he regains strength. Fever may occur at the onset of a relapse and then gradually disappear.

#### PHYSICAL EXAMINATION

The general appearance, the sallow muddy face and pigmented knuckles frequently give a clue. The appearance of the tongue and mouth is described above, and the anæmia is described later.

The skin may be dry and scaly over the forearms and legs. There may be evident signs of loss of weight. In advanced cases, there is œdema of the feet due to hypoproteinæmia. The

œdema I have observed to disappear with the use of nicotinic acid alone (oral and parenteral).

The abdomen may be normal in contour and consistency in early cases, but in more advanced cases there is wasting of the subcutaneous fat, and the intestines are outlined against the parietes. Gurgling of the intestines may be audible and palpable. The abdomen may be distended and tympanitic on percussion.

In 44 cases out of 50, it was noted that the descending colon and cæcum were not palpable. In 6 patients giving a clinical history of dysentery, the colon was felt thickened and tender. A low blood pressure was frequently observed during relapses (e.g. readings of 90 mm. Hg. systolic and 60 mm. Hg. diastolic—or 110 mm. Hg. systolic and 65 mm. Hg. diastolic).

*Varieties of syndrome.*—It is important to realize that for every fully-fledged case as described above that is seen, there may be several cases met with which exhibit only part of the syndrome. These may be called 'larval forms' or 'formes frustes'.

There may be glossitis, anæmia and constipation. The patient may complain of indigestion and gurgling and loss of weight, but gives no history of diarrhœa. There may be only anæmia, blackness of the skin and debility; or glossitis and loss of weight only. Any such combination of symptoms may be met with. Such cases are only too commonly labelled as anæmia, debility, neurasthenia or indigestion, and the true significance of the vitamin B deficiency is missed.

#### *Biochemical and pathological features*

*Hæmatological findings.*—The anæmia is typically of the megalocytic type.

In 5 cases, the size of the red cells was measured by Eve's halometer.

In 3 cases, the size was 8 microns and in 2 cases 8.2 microns.

The colour index was in most cases 0.9 or higher.

2 cases	showed a colour index of	0.7
6 "	" " " " " "	0.8
9 "	" " " " " "	0.9
4 "	" " " " " "	1.0
11 "	" " " " " "	1.1
1 case	" " " " " "	1.3
3 cases	" " " " " "	1.4
1 case	" " " " " "	1.5

A typical blood picture is as follows:—

Patient, male—		
Hæmoglobin	.. ..	58 per cent
Red corpuscles	.. ..	3,100,000
Colour index	.. ..	1.0
White corpuscles	.. ..	5,950
Polymorphs	.. ..	65 per cent
Lymphocytes	.. ..	34 "
Mononuclears	.. ..	1 "

Marked anisocytosis and poikilocytosis. Many megalocytes showed hyperchromia. Basophilic degeneration. A few microcytic cells. No normoblasts nor megaloblasts.

A patient was admitted in a very advanced state of anæmia. He had lost 50 lb. in weight

and was very emaciated. Blood transfusion was done but he only temporarily revived and succumbed soon afterwards. His blood picture was as follows:—

Hæmoglobin	.. ..	25 per cent
Red corpuscles	.. ..	910,000
Colour index	.. ..	1.5
White corpuscles	.. ..	3,800
Polymorphs	.. ..	34 per cent
Lymphocytes	.. ..	50 "
Mononuclears	.. ..	16 "

Severe anisocytosis and poikilocytosis, slight hypochromia with a tendency to enlargement of cells. No normoblasts nor megaloblasts.

In such advanced cases of anæmia, the absence of regenerative cells is explained by the aplastic degeneration of the bone marrow. The fatal conclusion even after a blood transfusion is due to the same aplasia.

#### *The gastric secretion*

There may be absolute achlorhydria or hypochlorhydria. In 7 cases, absolute achlorhydria was found, and in 5 cases a marked hypochlorhydria. Two cases showed a practically normal curve.

*Glucose tolerance.*—The glucose tolerance test after ingestion of 50 grammes of glucose shows a flattened or delayed curve due to deficient absorption of glucose from the small bowel. A typical curve is as follows:—

Resting blood sugar	..	90 mg. per 100 c.c.
One hour after glucose	..	130 " " 100 "
Two hours after glucose	..	85 " " 100 "

*Sigmoidoscopy.*—The typical appearance in an uncomplicated case of the syndrome is a pale, thin-walled mucous membrane of the rectum.

In several cases, scrapings of the mucosa were taken directly via the sigmoidoscope and examined for ova and cysts, always with negative results.

In an acute relapse, the rectal mucosa may be reddened and œdematous and covered with mucus. In such cases, a difficulty in diagnosis may arise, and the appearance suggests at first ulcerative colitis. A scraping will be negative for cysts and amœbæ. The diagnosis is determined by the therapeutic test. As the glossitis subsides and the general condition of the patient improves, the rectal congestion settles down.

*Fæces.*—In sprue, the stools have a high total fat content varying from 25 to 60 per cent of the dried fæces. The fats are split normally as there is no deficiency of enzymes but the fats are not absorbed. The neutral fats to the fatty acids and soaps are as 1:3.

The estimation of neutral fat, fatty acids and soaps by laborious laboratory methods is not necessary. The presence of excessive fat in the stools can be satisfactorily recognized by microscopical examination alone.

In the syndrome I am describing, there may be no increased content of fat. Under the

microscope, occasional fat cells and fatty acid crystals may be seen, but they are not present in any marked degree. There is evidence of undigested food with no increased fat.

I have however seen stools exactly like those of classical sprue, pale, frothy, bulky stools, full of fat and fatty acids, in patients who exhibited no other recognizable feature distinguishing them from the syndrome under discussion.

I can only come to the conclusion that the two conditions are closely related. The difference may be in the preponderance of carbohydrate in the Gujrati diet compared with the mixed diet of Europeans in whom sprue is classically described—or in some particular deficiency of the vitamin B complex resulting in a variation of the syndrome.

### *The onset of the condition*

*The onset may be insidious*, the initial symptoms being progressive weakness, anæmia and loss of weight. The patient complains that he is getting weaker day by day; and often notices that his skin is getting black. The skin overlying the knuckles of the fingers looks darker than normal, and his complexion is sallow and muddy. There may be darkness of the skin around the neck and the lips. The patient is conscious and concerned about his blackness, and realizes he is suffering from some obscure disease. He feels weak and disinclined to work, his appetite fails, and he loses weight from no apparent cause. The tongue may be sore at this stage, or glossitis may precede other symptoms by a long period. Then, after some time, he begins to get diarrhœa. There is gurgling in the abdomen, and irregular loose motions are passed. As the disease progresses, digestion becomes more and more disturbed. At this stage the diet is usually limited to buttermilk, as is always prescribed by indigenous practitioners. Often the patient will exist for months on buttermilk only.

As soon as heavier food is taken, the patient complains that he gets borborygmi and diarrhœa, and so he hesitates to add anything more to his diet. This extremely limited diet eventually leads to other dietetic deficiencies, and to a state of nutritional œdema due to hypoproteinæmia.

*The onset may be precipitate* with vomiting and diarrhœa. Often the patient will attribute the attack to the water of some place he may be residing in, e.g. Bombay, or it may have commenced while on pilgrimage, the strain and fatigue associated with which probably being the determining factor.

The diarrhœa weakens the patient. He rapidly loses weight. Glossitis may set in at the same time, or shortly afterwards, or may precede the attack.

The diarrhœa subsides for a time with treatment, only to relapse every two or three months.

### *Varieties of onset*

Onset with—				
Diarrhœa	..	..	..	7 cases
Diarrhœa and glossitis	..	..	..	3 "
Glossitis	..	..	..	6 "
Anæmia	..	..	..	4 "
Pregnancy	..	..	..	13 "
Malaria	..	..	..	10 "
Dysentery	..	..	..	7 "
				50 cases

### *Precipitating factors*

*Pregnancy* is cited as a precipitating factor in 13 cases.

A common history is that the patient develops diarrhœa, or what she calls dysentery, in the last month or so of pregnancy. There may be some blood and mucus in the stools, or there may be only watery motions. The diarrhœa may persist for some time after delivery, and all the symptoms associated with the syndrome we are discussing develop, *viz.* glossitis, anæmia, loss of weight, etc. The diarrhœa may relapse with each pregnancy, the patient having more or less normal health in between pregnancies.

(1) *Case 13.*—Female, age 35 years, Patel caste.

Diarrhœa commenced one month before delivery. Also with 2 previous pregnancies—normal health in between. Diarrhœa 10 to 20 motions a day—watery with mucus. Lienteric in type.

Glossitis, pain in throat on swallowing. Burning palms and soles and substernal. Dryness and blackness around mouth and feet and knuckles. Angular stomatitis present.

Tongue clean, red spots at tip. Dyspepsia—gurgling. Distension, achlorhydria. Loss of weight. Abdomen distended and thin walled. Hæmoglobin 32 per cent. Total red cells 1,400,000. Colour index 1.1.

(2) *Case 7.*—Muslim female, age 28 years.

Glossitis since childhood.

Diarrhœa, watery motions, yellow, copious, lienteric. Always worse with pregnancy—4 children. Glossitis, fiery red tongue, stomatitis and pharyngitis, pain in throat on swallowing.

Tongue glazed, clean, pale. Burning palms and soles and substernal. Pigmentation of lips and angles of mouth. Abdomen—tympanitic, visible peristalsis, gurgling. Loss of weight. Hypochlorhydria. Hæmoglobin 62 per cent. Red cells 3,216,000. Colour index 0.9.

(3) *Case 32.*—Female, Bania, age 35 years, 3 pregnancies.

Diarrhœa with first pregnancy diagnosed as sprue—no glossitis then—sick for 6 to 7 months.

Constipation with second pregnancy.

Third pregnancy during last month, diarrhœa with blood and pus for 7 days and then after delivery diarrhœa continued as watery, yellow motion without blood and pus. Gurgling and glossitis now appeared.

Glossitis—clean tongue, pale.

Skin—very black back hands and all way up arms to axillæ—very dry black skin and face and lips in front of knuckles. B.P. 110/70.

Marked loss of weight. Abdomen—distended, thin walled. Gurgling, flatulence, heartburn, vomiting. Hæmoglobin 28 per cent. Total red cells 1,232,000. Colour index 1.1. Glucose tolerance 110—180—100. Hypochlorhydria.

*Discussion.*—These cases differ in no way from the other cases not associated with pregnancy. They are not examples of tropical megalocytic anæmia of pregnancy.

In tropical megalocytic anæmia, the gastric secretion is normal in most patients and

diarrhoea is quite rare (*British Encycl. Med. Practice*, Vol. I, p. 439). In the 3 cases detailed above, the outstanding clinical feature is the diarrhoea. Aehlorhydia was found in one case and marked hypoehlorhydia in 3 cases. They therefore resemble clinically the syndrome under discussion, and not tropical megalocytic anaemia. It is recognized that in pregnancy, there is an increased demand for vitamin B. These patients are probably living on the threshold of vitamin B deficiency. The added strain of pregnancy just tips the scale in the adverse direction, so that now there is a definite deficiency of vitamin B.

Fever is mentioned in 10 cases as one of the initial symptoms. Malaria may precipitate the syndrome in one who is on the border-line of vitamin B deficiency. The extra metabolic strain imposed by the attack of malaria results in a breakdown of the defences.

(1) Case 48.—Female, Bania, age 25 years.

First had malaria fever for one week—and then diarrhoea commenced—watery white motions—with glossitis. Admitted as a typical case with glossitis, angular stomatitis, rough dry scaly skin of legs, anaemia. Haemoglobin 50 per cent. Red cells 2,814,000.

Dysentery is frequently mentioned by the patients, but the term is a clinical one only, not verified in the majority of cases by laboratory methods.

In only 2 out of 50 cases were *Entamoeba histolytica* cysts isolated. No bacteriological examinations were made to isolate the organism of bacillary dysentery. Blood and pus are at times reported by the patients, but their mere presence in the motion is not necessarily indicative of dysentery. Blood and pus may be due to piles or to straining due to the excessive diarrhoea or to pelvic congestion due to pregnancy. Blood and mucus may also be passed in an acute relapse of the syndrome, when the whole alimentary mucous membrane from the mouth to the anus is in a state of congestion. The tongue is red and raw, the pharynx is inflamed, there is dysphagia and heartburn probably due to a similar rawness of the oesophagus. Sigmoidoscopy in such a condition will reveal an oedematous, red, rectal mucous membrane covered with mucus.

In 7 of the 50 cases, there seems to have occurred a definite attack of amoebic dysentery. I do not think there is any argument in support of the theory that dysentery is the cause of the syndrome. The relationship can be explained in terms of a conditioned deficiency. Dysentery is essentially a large bowel disease, whereas this syndrome is a small bowel dysfunction. Patients who have suffered from dysentery, and notoriously Gujrati patients, diet themselves most rigorously over very prolonged periods. They exclude all vegetables and the richer cereal foods from their diet, and live only on curds and congee and dhal water. The dietetic restriction may be voluntary and therapeutic, or it may be enforced by the patient's inability to take heavier food, or

by his lack of appetite. The primary dysentery symptoms, due to a large bowel lesion, are loose motions containing blood and pus, abdominal colic, weakness and loss of weight. With the switchover to a small bowel dysfunction, due to a conditioned vitamin B deficiency, symptoms due to jejuno-ileal insufficiency become paramount. The nature of the stools alters, the blood and pus disappear and the motions become watery and copious. The patient complains of gurgling and an urgent desire to defaecate after food. Soon anaemia and glossitis and a feeling of exhaustion set in. Several patients have clearly described this transition from large bowel to small bowel pathology in recounting their history. As one patient remarked 'Dysentery stopped and sprue began'.

(1) Case 29.—Male, age 33 years, Patel caste.

Dysentery (clinical diagnosis only) 5 years ago blood and pus—dysentery lasted 2 months—20 to 25 motions a day.

Then the bowel motions less, with no blood and pus. Gurgling and swelling of the abdomen commenced, and glossitis started one month ago.

Motions 7 to 8 a day—watery and yellow—any time of day—exhaustion after motion. General sallowness of skin of face, back of hands and shins.

B.P. 80/40. Tongue clean, glazed. Abdomen—distension, thin-walled, gurgling. Loss of weight. Wasted skin. Hypochlorhydia. Colon thick and tender. Haemoglobin 44 per cent. Total red cells 1,944,000. Colour index 1.1. Sigmoidoscopy—normal mucous membrane except for pallor.

Treatment—Patient improved greatly on nicotinic acid, liver extract, hydrochloric acid and fersolate. Increase of weight 11 lb.

Sex.—In a series of 50 cases, 30 were in males. The condition shows no preference for either sex.

Age.—The age of the patients varied from 20 to 40 years. In a few cases, patients of 50 years and over presented themselves with the syndrome, but in such cases a careful history elicited the fact that they had suffered from the same condition many years previously, and this attack was but a recrudescence.

Caste.—In the series of 50 cases, 11 were Muslim and 39 were Hindu. This is of no significance, as the population varies in the same degree. Of the Hindu patients, 11 were Brahmin, 12 were Bania, 3 were Patel, 2 were Jains, 1 Soni; there were no cases from the depressed classes. This observation may be of some significance. The higher caste eat more wheat and polished rice, the lower caste subsist more on bajri and coarser grains and often eat home-pounded rice which has a considerable content of vitamin B.

#### Acute relapse

This is exemplified by the following two cases:—

Case A.—Muslim male, aged 24 years.

History of diarrhoea for 10 months. Acute glossitis for the last 10 to 15 days—tongue fiery red glazed patches on the dorsum. Whole pharynx inflamed, so that he is unable to eat food.

Diarrhoea, 4 to 5 profuse watery yellow motions, marked exhaustion after motions—motions passed at all times of the day.



No history of dysentery. B.P. 100/50. Marked loss of weight, and strength. Achlorhydria—absolute. Dyspepsia—gurgling and distension and heartburn. Blood. Hæmoglobin 62 per cent. Rêd cells 2,616,000. Leucocytes 64,000. Colour index 1.1. Size of red cells 8 microns.

Sigmoidoscopy—very œdematous, reddened, gelatinous, mucous membrane. Liquid white fœces with much mucus.

Treatment—immediate relief in 24 hours with nicotinic acid. The redness of the tongue disappeared and patient was able to swallow the Ryle's tube for gastric analysis.

Case B.—A Hindu patient presented himself for examination with what I considered the typical syndrome of this variant of sprue. To my surprise he came again in a few days with what he described as dysentery. He was pouring bloody stools and was too weak to stand. His tongue and mouth were fiery red and he was unable even to drink fluids. In spite of the bloody stools, I adhered to my original diagnosis. I prescribed only nicotinic acid by mouth and injection. In 24 hours there was marked improvement and by 48 hours all blood had stopped. Sigmoidoscopy revealed a red, swollen, gelatinous mucous membrane, covered with mucus. I came to the conclusion that his whole intestinal tract was injected and inflamed right from his lips to his anus.

The patient made steady progress with treatment only for the sprue syndrome and without any amœbicidal measures.

### Treatment

The main object in treatment is to supply the vitamin B complex orally and parenterally.

*Baker's yeast* is obtained fresh every day from a local baker and given to the patients in quantities of half an ounce three times a day.

*Peanut butter* is advised. The patients are instructed to grind up fresh peanuts finely and add a little peanut oil till it is of the consistency of butter. Spies *et al.* recommend a mixture containing 25 per cent dried brewer's yeast, 64 per cent peanut butter and 8 per cent peanut oil. The peanut contains about 25 to 30 per cent protein, 40 to 50 per cent fat and 10 to 20 per cent carbohydrate. It is a rich source of vitamin B complex.

*Wheat bran* is made into a porridge with milk. Proprietary products such as marmite and bemax are almost unobtainable nowadays due to the war.

*Nicotinic acid* at once relieves the glossitis and stomatitis, and also controls the diarrhœa. Given in maximum doses by mouth and by injection, a patient miserable with glossitis and dehydrated with diarrhœa can be transformed in 24 to 48 hours. The dramatic relief confirms one in the belief that nicotinic acid deficiency is responsible for at least part of the syndrome.

*Riboflavin*.—Certain cases of glossitis do not respond to nicotinic acid. If the sore tongue does not improve with the latter therapy, then a few injections of riboflavin (lactoflavin) may produce a beneficial change.

The whole vitamin B complex may be prescribed in convenient form as manibec, multivitaminon, or B-G-phos elixir, to name a few proprietary products which have been tried with success.

*Hydrochloric acid* is given if there is hypochlorhydria. It may be combined with judicious doses of tincture of opium if there is diarrhœa.

A useful formula is :—

Acid hydrochloric dil.	..	..	30 minims
Tincture opii	..	..	10 "

Water to half an ounce.

Half an ounce three times a day.

*Pulv os sepia* (*Batavia powder*) is very helpful in controlling diarrhœa if persistent.

*Liver extract* is indicated for three reasons: it supplies the hæmopoietic factor which is deficient in megalocytic anæmia; it is a rich source of vitamin B complex; it improves the absorption of amino-acids from the small intestine.

Crude liver extract gives the best results. Preparations such as campolon, hepatex T, hepolon, plexen are used in large doses daily or on alternate days.

*Iron* is necessary to overcome the anæmia. It is particularly difficult to administer iron, as it tends to aggravate the diarrhœa. Ferri et ammon citrate especially will frequently cause an attack of diarrhœa in a patient otherwise doing well. If a covering dose of tincture of opium is given with the ferri et ammon citrate, the latter may be tolerated. Another method is to give pil ferri redactum 5 grains three times a day, or fersolate or ribothiron tablets.

*Ultra-violet light* has been found helpful in toning up the system generally, and has been frequently prescribed.

*Tongue*.—Two per cent chromic acid applied to the tongue relieves the glossitis.

*Diet*.—The classical indigenous treatment is buttermilk and curds.

I have seen a patient live solely on buttermilk of which he drank 12 seers a day. He increased in weight by 30 to 40 lb.

In early cases, this treatment is advised: buttermilk, fruit juice, mashed up bananas and tea constitute the sole diet. Later, rice and milk, curds and kigdi and pulse water and bajri are added. Ghee and all fried foods are rigidly forbidden. In Muslim patients, liver soup and minced meat are advised from the beginning.

*Sprulac* (Cow and Gate), a specially prepared dried milk powder with diminished fat content, is a very valuable foodstuff, but it has not been used in this series.

A note on *nicotinic acid therapy*.—Nicotinic acid alone frequently dramatically relieves not only the glossitis, but also the vomiting and diarrhœa. Three cases quoted below were treated on admission with nicotinic acid only. In 2 or 3 days, the loose diarrhœa was controlled, the tongue was relieved, and the œdema lessened. Then other treatment was added to improve the blood. The improvement with nicotinic acid alone lends considerable weight to the hypothesis that deficiency of the vitamin B complex is one of the causal factors in producing the syndrome.



Case 1.—Male, Brahmin, age 40 years.

Previous history.

- (i) Onset 1937—gradually progressive mental and physical depression accompanied by anaemia. Treated in hospital for 1½ months.
- (ii) Relapse 1939—weakness, vomiting and diarrhoea, loss of weight, anaemia. Cysts *Entamoeba histolytica* present in faeces—treated with enterovioform, hepatex T, campolon, plastules—recovered.
- (iii) Relapse every following monsoon with weakness, anaemia, depression, loss of weight and diarrhoea. Glossitis recurred each time now with the attack of diarrhoea.
- (iv) 1942. Admitted to hospital again with weakness, tingling soles of feet and palms of hands, diarrhoea and anaemia. Tingling became a prominent symptom; treated with hydrochloric acid, hepolon, nicotinic acid, iron, hepatex T and berin. All the symptoms subsided except the complaint of tingling. His legs felt stiff and he experienced difficulties in walking. The knee reflexes were absent.
- (v) Monsoon 1943. Admitted again in a very debilitated state. He complained of:—
  - (a) Prostration.
  - (b) Vomiting.
  - (c) Diarrhoea. Watery, yellow motions—7 or 8 a day—passed at any time of day or night.
  - (d) Sore tongue and throat.
  - (e) Tingling of hands and legs.
  - (f) Loss of weight.
  - (g) Slight fever.
  - (h) On physical examination the following clinical features were noted:—
    - (a) Tongue—dry, clean, raw red with glazed patches on dorsum. No angular stomatitis.
    - (b) Sallow complexion. Muddy appearance. Skin of knuckles of fingers blackish.
    - (c) Marked anaemia.
    - (d) Abdomen—normal contour. Liver not enlarged, colon not palpable nor tender.

Laboratory findings:—

- (a) Absolute achlorhydria.
- (b) Faeces—no cysts present and no ova.
- (c) Blood—red corpuscles 1,326,000.
- (d) Haemoglobin 30 per cent, colour index 1.1. Size of red cells 8.2 microns.

On admission the patient was given only nicotinic acid tablets and injections of nicotinic acid twice a day intravenously. The effect was most striking. With two injections of nicotinic acid, the vomiting was controlled and the tongue felt and looked better and the motions were reduced from 8 to 4. The next day, on the same treatment the motions were reduced to three and on the third day, he passed one hard motion only. The motion was formed and digested. The tongue looked much better, the patient's general expression was much improved, and he felt distinctly better.

After 3 days on nicotinic acid only, the patient passing one motion a day only, the treatment was amplified. Baker's yeast, fersolate tablets and hepolon injections were given. Hydrochloric acid was administered because of the achlorhydria.

**Discussion.**—The whole syndrome from the beginning is attributable to vitamin B complex deficiency.

There is a superficial resemblance to sprue, and locally the indigenous practitioner calls such

cases sprue. But the stools in this case never approximated to those characteristic of sprue. The motions were always watery yellow or like curds with no increased fat content. It is true that *Entamoeba histolytica* cysts were detected in faeces on one occasion, but this finding was never confirmed later. The glossitis and macrocytic anaemia and the achlorhydria are not typical of chronic dysentery.

The response to nicotinic acid therapy was most dramatic, and confirms one in the belief that nicotinic acid deficiency lies at the root of the trouble. The complaint of tingling and stiffness in walking points to a thiamine deficiency, although vigorous treatment with thiamine preparation did not alleviate the symptoms.

#### PROGRESS UNDER TREATMENT

As the patient improves, the gurgling in the abdomen disappears, the motion becomes better formed and the patient looks healthier and brighter. There is visible a distinct change in his facial expression. Not every case, however, steadily improves. The stools may become constipated but the blood does not seem to improve. In spite of intensive liver extract therapy, there is no progress in the blood condition. This is always disappointing to both doctor and patient. It is probably due to hypoplasia of the bone marrow.

There may be actual aplasia of the marrow and such cases steadily deteriorate to a fatal conclusion.

At times one meets with an intractable diarrhoea. No amount of sedatives, opiates or vitamins will check the diarrhoea. The motion becomes profuse, incontinent and the patient becomes collapsed and oedematous, and dies. This is probably explainable as a state of jejuno-ileal insufficiency which has become so advanced as to be irreversible and unresponsive to all remedial measures.

Relapses frequently occur, even after many years. I have met a patient who had his first attack in 1917, with a relapse in 1924 and again in 1943. In the intervening years, he was quite well.

Relapses occur frequently in the monsoon and winter. Some patients say they relapse every year in these seasons.

#### DIFFERENTIAL DIAGNOSIS

**Amoebiasis.**—I have repeatedly seen patients referred with the diagnosis of amoebic dysentery. As one swallow does not make a summer, so the occasional discovery of a cyst of *Entamoeba histolytica* does not constitute amoebiasis. The syndrome as a whole must be studied.

In amoebiasis, the anaemia is seldom severe and is always secondary and microcytic. Glossitis does not occur in amoebiasis. The liver tenderness and thickened colon point to amoebiasis, rather than sprue. The mental sluggishness and debility and constitutional upset are more suggestive of the sprue syndrome.

Achlorhydria and a flat glucose curve denote the small intestine disturbance typical of the sprue syndrome. Above all, the sigmoidoscopic appearance should clinch the differential diagnosis.

*Tuberculosis of the abdomen.*—Glands in the neck, a family history, fever, an old history of pleurisy may serve to give the clue to the diagnosis of tuberculosis.

*Pellagra.*—Pellagra is not uncommonly met with in Gujerat. Full-fledged cases may be seen with the classical pigmentation of the back of the hands and the front of the ankles. In my experience, diarrhoea is uncommon, the patients usually complaining of constipation.

The glossitis is much the same as in the sprue syndrome. The pigmentation of pellagra is a rash on the skin which can be removed by keratolytic ointments. In sprue the pigmentation is in the skin and is only a deepening of the normal pigment and is not a rash.

### Summary

A syndrome commonly occurring in Gujerat is described which differs from sprue as described in textbooks of tropical medicine only in the nature of the stools. The stools are nearly always watery and passed at any time of the day.

The syndrome is believed to be a variant of the sprue syndrome, the nature of the stool being conditioned either by (a) the predominantly carbohydrate nature of the diet or by (b) some particular deficiency of the vitamin B complex.

The syndrome is believed to be due to a primary dietetic deficiency of the vitamin B complex leading to jejuno-ileal insufficiency.

The syndrome is relieved by therapy supplying the vitamin B complex orally, and parenterally.

Thirteen cases are quoted in which the syndrome was precipitated by pregnancy.

An explanation is offered as to the mechanism of the syndrome being implanted on dysentery. A conditioned deficiency of vitamin B due to dietetic restriction or defective absorption leads to jejuno-ileal insufficiency. It is possible to trace the change-over from a colitis to a small bowel disorder.

Acute relapse of the syndrome mimics dysentery. Sigmoidoscopic appearance typical of a relapse is described.

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## Medical News

### FEEDING OF CHILDREN IN WAR-TIME

#### SUBSTITUTES FOR IMPORTED FOODS

A COMMITTEE of experts appointed by the Indian Research Fund Association to suggest satisfactory substitutes for imported infant foods and breakfast cereals has issued a pamphlet on the feeding of children from six months to six years in war-time.

The committee has dealt with the problem of feeding in general apart from the present war emergency. Alternative methods of feeding which would ensure good health and development have been discussed without reference to their cost.

The pamphlet deals with nutritional requirements of young children, planning the child's diet, weaning and diets suitable at different ages. In planning the diet of the growing child, it says, the first essential is to ensure that sufficient quantities of body-building and protective foods are included. Once requirements in this respect are fulfilled, a healthy child's appetite will determine its intake of energy-producing foods.

All the three categories of foods have been tabulated and the requirements of children from six months to six years are given with the planned diet for all meals.

Apart from the general principles of feeding, the pamphlet also deals with the palatability and attractiveness of meals and gives hints for their preparation and cooking. A few recipes for soups and other preparations are included in the pamphlet which is being distributed by the Indian Research Fund Association Office, New Delhi, and the Maternity and Child Welfare Bureau of the Indian Red Cross Society.

### THE SIR NILRATAN SIRCAR FUND

THE Calcutta Medical Club has decided to perpetuate the memory of the late Sir Nilratan Sircar, Kt., M.A., M.D., D.C.L., LL.D., the founder and as first president, by instituting a Fund of Rs. 25,000 from the interest of which, as a first step, will be created an Annual Oration called Sir Nilratan Sircar Memorial Oration which will be delivered annually, at the Calcutta Medical Club, by a medical man of outstanding abilities from all over India. The Committee appeal to the public to donate to the above Fund, which should be sent to the Honorary Secretaries, Calcutta Medical Club, C.M.C. House, 91B, Chittaranjan Avenue, Calcutta.

## Public Health Section

### LEPROSY CONTROL

#### WITH PARTICULAR REFERENCE TO THE MADRAS PRESIDENCY

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#### Introduction

'THERE was a time when tuberculosis was regarded as a disgrace and the unfortunate victim was ashamed of his affliction. Consumption somehow cast a stigma upon its victim. The social background was little understood and the public thought that people suffering from consumption were somehow blameworthy' (Clarke, 1933).

An article on the control of leprosy could not commence better than with the above quotation. Syphilis, tuberculosis and leprosy are the three diseases which for many decades have been under a social stigma, and of these diseases leprosy least deserves the opprobrium which has been showered upon it. Therefore, before considering the question of the prevention of leprosy, it would not be out of place to make a plea that medical men in their speaking and thinking should adopt the recommendation of the leprosy conference held at Manila in 1931 and drop the word 'leper' from their vocabulary. I stress this particularly for it is not the patients against whom we are fighting but the disease. Leprosy, as far as public health is concerned, is primarily a medical and preventive problem and secondarily a social one. There is the social aspect of the leprosy just as there is the social aspect of infantile paralysis, rheumatoid arthritis, or any disease or condition which produces deformity or disfigurement, but there is no reason why a word should be used which carries with it the taint of disgrace. A very different outlook is now seen in tuberculosis, and the word 'consumptive' has largely disappeared from medical literature. In general, a patient is described as suffering from a certain disease, and a noun is not used descriptive of the patient, and therefore there is no fundamental reason why the noun 'leper' should not also be relegated to the past.

The work of the past eight years has seen the completion of the preliminary steps in the organization of the campaign against leprosy in the Madras Presidency, and it is now possible to consider a more comprehensive policy which aims at setting up a system of control within the next two decades. Once leprosy is brought under an efficient system of prevention, then it will only be a matter of time before the disease is eliminated. Since any system established will be applicable with local modifications to

all areas, it is thought that a sketch of the suggested future developments of the leprosy campaign in Madras might make a useful contribution to leprosy control in general, and it is with this end in view that this article is published.

It is of interest to note that the routine treatment of leprosy is now accepted by the authorities as a proper function of the general medical service of the Presidency, and that it is now agreed that if a patient has leprosy, he has as much right to receive treatment at a general hospital as has a person suffering from tuberculosis, cancer or syphilis. Therefore, at all Government and Mission hospitals and at Local Fund dispensaries, treatment for leprosy should be available. If the number of cases warrants it, a special clinic should be organized, but all clinics which are primarily for the routine treatment of the disease, should be, and in Madras generally speaking are, under the control of the District Medical Officer (Civil Surgeon). A further advance in the preliminary organization of the leprosy campaign was made when an order from the Surgeon-General's department was issued making it incumbent upon all district hospitals to admit patients suffering from leprosy who require immediate medical or surgical treatment, either for diseases other than leprosy or for acute complications due to leprosy. It is advised that these patients should be admitted into the septic or infectious diseases wards if infective or septic, and into the ordinary wards if not infective.

Another milestone towards the establishment of an adequate anti-leprosy campaign was passed when a special leprosy department was organized in the General Hospital, Madras. Similar departments are under organization in the other teaching hospitals of the Presidency. Special leprosy investigation units have been developed in the Presidency, which cover urban, rural and child leprosy, and research work is being continuously undertaken at the Lady Willingdon Leprosy Sanatorium in co-operation with the King Institute, Guindy, and the pathological department of the Medical College, Madras. Post-graduate courses of 14 days' duration are organized, but the experience of the past six years indicates that this is too short a period.

It is our firm belief that leprosy can be controlled, but adequate finance and a properly equipped and sufficient medical personnel must be available. This fundamental point will be repeatedly emphasized, since half-hearted measures are of little value in dealing with the leprosy problem. In the past, the building of a few institutions, with emphasis on the philanthropic and social side of leprosy, and the establishment of out-patient centres were

considered sufficient. An age-long problem such as leprosy demands the attention of the best qualified in the profession, and an expenditure of money which will reach many lacs. All this means that in future leprosy workers must be paid salaries comparable to other research workers, and doctors of similar grade of training and experience.

It has been realized for some time and was strongly emphasized in 'The report on leprosy and its control' (Central Advisory Board of Health, 1942) that leprosy cannot be controlled by treatment. Therefore, treatment will play only a limited part in the campaign, and thus it will be understood that a leprosy policy based mainly on the establishment of out-patient centres can never be successful. It should be stated, lest the position be misunderstood, that treatment is of value for three reasons:—

(a) In certain types, especially the early lepromatous variety, it is believed that not only is treatment beneficial, but all the evidence at present available indicates that the earlier and the more intensive the treatment the greater is the chance of recovery.

(b) By making treatment available, patients are more ready to submit to the necessary preventive measures.

(c) Many cases can only be kept under observation by regularly attending a treatment centre.

#### *The anti-leprosy scheme*

With these introductory remarks we are now in a position to discuss the measures which should be adopted in any comprehensive anti-leprosy scheme; these will be briefly considered under the following heads:—

- (1) Institutions.
- (2) Teaching.
- (3) Survey.
- (4) Rural leprosy.
- (5) Urban leprosy.
- (6) General hospitals and out-patient clinics.
- (7) Children's sanatoria.
- (8) Deformed and derelict cases.
- (9) Beggar problem.
- (10) Research.
- (11) Propaganda.
- (12) Place of voluntary organizations in the anti-leprosy campaign.
- (13) Legal measures.
- (14) Conclusion.

#### *Institutions*

The question of the place of institutions in the anti-leprosy campaign is discussed first, because without adequate institutional accommodation a complete anti-leprosy system is impossible to organize. The approach to this aspect of prophylaxis may be best illustrated by particular reference to the Madras Presidency, remembering that while principles remain, it is details which modify the putting of the principles into action. These details depend on different environmental, social and other factors.

As far as can be ascertained at present, leprosy is an important endemic disease in the following districts of the Presidency: Chingleput, North and South Arcot, Trichinopoly, Vizagapatam, East and West Godavari, Salem and Malabar. It is our firm belief that the aim should be to establish a leprosy institution for the treatment and segregation of open cases in all districts where leprosy is found to be a serious disease. While it may be impossible to cope with all cases which present themselves for treatment, it is undoubtedly preferable to isolate as many infective cases of leprosy as possible in institutions, for this is the most effective form of isolation. Further, as far as possible, admission to institutions should be confined to cases in the following categories:—

1. Early lepromatous cases (infective) who are liable to pass on to the more advanced stage unless given institutional treatment.
2. Infective cases whether early or late in whose house there are young children liable to be infected.
3. Acute conditions needing hospitalization might be admitted temporarily when there is a bed available, or if the patient is unable to go to a general hospital.
4. All active cases among children whether open or closed.

At present there are institutions in Chingleput, South Arcot, Vizagapatam, East and West Godavari, and Malabar. Therefore, with the consent of the managing body of the existing institutions, which is generally the Mission to Lepers, steps should be taken to enlarge, and where necessary modernize, the institutions in the above districts, and new institutions should be considered for North Arcot, Trichinopoly and Salem districts. While it is accepted that institutions alone will not solve the problem, yet without institutions the leprosy campaign in a district is liable to be ill-balanced. Therefore, institutions should be available for isolation of those cases which voluntarily present themselves for segregation. District survey officers should keep in close touch with these institutions so that they may be familiar with the practical methods of leprosy, diagnosis and treatment. Plans for these institutions, and new institutions for North Arcot, Salem and Trichinopoly should be devised, so that they will each accommodate 300 to 400 patients and have the necessary medical and nursing facilities. At least two doctors would be required, and a reasonably well-equipped hospital should be part of these institutions. Occupational therapy such as weaving, carpentry, etc., should be available, with an adequate amount of land for agricultural purposes. Where there is an institution already in the district, it should, if possible, be brought up to the necessary standard of efficiency rather than an entirely new institution established.

In addition, the Lady Willingdon Leprosy Sanatorium should be so developed that it could adequately fulfil its function of being the centre of the provincial leprosy campaign and the premier institution in the Presidency. Details of

these developments need not be specified, but should include better facilities for post-graduate work and hostel accommodation for post-graduate students. No scheme of leprosy control is likely to succeed unless one of the institutions in the province is developed to such an extent that all aspects of research, treatment and training can be adequately covered and co-ordinated in it.

### Teaching

The place of teaching in the leprosy campaign is discussed now, because the greatest barrier to progress is the lack of realization among the medical profession that leprosy is first a medical problem and secondarily a social one. Until leprosy is given its right place in the thinking of all medical men, especially of administrative public health officers, little headway will be made. There is a considerable fear that in plans for post-war reconstruction, leprosy control will be given cursory attention, for often those who plan for medical developments, relief and research are not themselves familiar with modern thought on leprosy, and their thinking is to a great extent influenced by their contemplation of leprosy as a beggar problem and a social problem. The teaching of the subject of leprosy, therefore, should be placed on an adequate footing. It can be stated that, except perhaps in the Madras medical colleges, nowhere is the importance of leprosy stressed. The teaching is usually a part of dermatology, and is left to a person who may be enthusiastic, but who neither from experience nor qualification is able to give that prestige to a subject which would ensure the interest and attention of the students. While a beginning has been made in Madras, it is impossible to do justice to the teaching of leprosy in the three medical colleges if one person is responsible for the organization of the whole work. Therefore, every medical college in areas where leprosy is an important endemic disease should have a separate leprosy department in the charge of a physician who has higher medical qualifications. The department should work in close association with that of dermatology, but leprosy should not be considered merely as part of dermatology, for then it would be given scant attention. Where leprosy is not an important disease in a province, then leprosy can be considered along with dermatology, but the lecturer should himself have taken an advanced course in training. The prevailing opinion that a fortnight's course in leprosy qualifies a person to become a leprosy expert should not be encouraged. A disease which has baffled mankind for centuries cannot be mastered in 14 days!

Post-graduate teaching in leprosy should cover the following courses:—(1) Elementary, (2) Advanced, (3) Refresher, (4) Specialist.

(1) *Elementary courses*.—These need not be for more than 14 days' duration and all practitioners should be encouraged to take at least this course.

(2) *Advanced courses*.—These should be open to all who have taken the elementary course and wish to

have a fuller acquaintance with the subject, and should be of a month's duration. All persons in charge of out-patient leprosy work should be encouraged to take this course as a very minimum.

(3) *Refresher courses*.—These should be for senior medical officers, health officers and school of medical officers and of 10 days' duration. The object of such an abridged course is not to train specialists, but to give district medical officers and those in administrative position up-to-date information so that they may be able to take a greater interest in the treatment and prevention of leprosy. Too often a leprosy clinic is established and a junior doctor is placed in charge, and the medical head of the district is unable to encourage or help because he knows very little about the subject. If such refresher courses as indicated were available, the doctor in charge of routine treatment of leprosy would receive encouragement and help, and leprosy treatment would become an integral part of the out-patient department of a district hospital, and not relegated to a shed in the back of the compound and given the minimum and scantiest attention. Health officers should be encouraged to take this course, so that they too may be in a better position to co-operate in any leprosy campaign.

(4) *Specialist courses*.—These should be for those who intend to specialize in leprosy and should be of 6 months' duration covering all aspects of the problem including the practical working and management of an institution. Such a comprehensive course should be taken by those who are in charge of leprosy institutions, survey units, teaching departments and any special investigation units. Only thus will men of adequate calibre be attracted.

### Survey

Muir (1931) many years ago stressed the necessity for survey units and developed the idea of propaganda, treatment survey parties. Since then widespread sample surveys have been conducted. In this connection the excellent work of Santra should be mentioned. While in the development of an anti-leprosy campaign survey is essential, the days for sample surveys, as far as the Madras Presidency is concerned, have passed. It is felt that no survey should be undertaken unless it has one of three objects in view: (1) as a basis for the organization of a preventive unit; (2) in order to ascertain whether leprosy is a serious disease in a given area; (3) to ascertain whether leprosy is diminishing or not in an area as a result of preventive measures. Type 1 (Lowe *et al.*, 1941) survey should be undertaken as a preliminary survey in fulfilment of the first two objects. Where a complete epidemiological survey or a follow-up survey is contemplated at least a type 2 survey should be undertaken, but preferably type 3. The following points should be stressed in the preliminary survey: (1) gross incidence; (2) child incidence; (3) child rate; (4) open case rate (*vide infra*). It is believed that a comparison of these figures will give a very fair idea as to whether leprosy is a serious endemic disease or not. In addition, careful attention should be paid to the percentage of cases in the various age groups, as we believe that an increase in the percentage of cases arising in the higher age group (15 to 34, 34 and above) indicates a satisfactory state and a tendency for the epidemic of leprosy to come under control. As stated elsewhere, it is our



belief that the epidemic of leprosy cannot be maintained in the absence of child infection (Cochrane, 1943).

In building up an anti-leprosy system, several survey units would be necessary. The staff should consist of the following as a minimum :—

- (1) A doctor, adequately trained in modern leprosy methods.
- (2) A clerk.
- (3) A lady worker, preferably an elderly lady, or if possible and suitable the wife of one of the members of the unit. (Santra who has had a great deal of experience in survey lays much stress on the necessity for a woman worker.)
- (4) A peon.

The doctor in charge of the survey party should have the necessary apparatus to undertake smear examinations and when necessary examine suspicious open cases, taking all slides back to headquarters, carefully numbering them for examination. One or more survey units should be organized in each district where leprosy is prevalent. Survey parties should not be sent out in a haphazard fashion, but only on reasonable evidence that leprosy may be a prevalent disease in a given area. All survey findings should be scrutinized by a specially trained officer, preferably the director of the leprosy campaign, who would decide whether active measures need be taken in a given district.

#### *Rural leprosy*

It is our firm conviction that leprosy can only be dealt with in rural districts by the establishment of rural units; these would correspond to the regional leprosaria which were established so successfully in the Philippine Islands. 'It is no use adopting an attitude, as is sometimes done, that isolation in India is impracticable and therefore other methods must be used. *There is no other method* which will replace isolation. What has to be done is to evolve methods of isolation which are suitable to Indian conditions'. With this statement in the Report of Leprosy and its Control in India we entirely agree. It can further be pointed out that isolation has hitherto been considered impracticable because, when authorities look at the problem in the mass, the size of it overwhelms them, and there is a general feeling of despair. If, however, it is realized that even in a highly endemic Presidency such as Madras, there are only certain areas where the disease is of such prevalence that active measures need be taken, and even in these areas there are only certain groups of villages where a segregation unit need be organized, then the question of isolation becomes a more reasonable proposition. As a result of the work of survey units, villages will be gradually discovered where measures need to be taken and an effective preventive scheme will slowly be evolved. Several methods of rural isolation have been suggested, but all such methods should have the aim of discovering the minimum amount of segregation necessary to control the disease. Ninety per cent of

persons in many rural areas are agriculturists who spend the greater part of the day in the fields, and so it may be that if measures are enforced to provide for night segregation, and thus keep infective cases away from their children at night, this one measure alone might reduce the chances of infection sufficiently for it to be increasingly difficult for the disease to spread. It might be helpful to describe briefly the rural leprosy prevention unit, organized in the Chingleput district, 23 miles south of Chingleput.

The staff consists of (1) doctor, (2) compounder, (3) nursing orderly, (4) gardener. Each member of the staff has a house at the centre and in addition there are the following buildings: (1) treatment clinic, (2) guest house, (3) laboratory, (4) store-room, and water tower which supplies the laboratory with running water.

On the other side of the road 6 cottages are built for night segregation of infective cases and in this area there is a well for the patients' use. Patients are given a  $\frac{1}{4}$  measure of rice a day and are required to come to the huts after their evening meal. It is granted that it may be unsatisfactory for patients to take their evening meal with the family and only later come for segregation, but after the war, if considered necessary, arrangements will be made for cooking or for the supplying of cooked food. If leprosy can be controlled by this amount of segregation, then the method has the merit of simplicity, for total segregation would necessarily involve compensation of the person segregated if he were the wage earner of the family.

Experimental rural units should be established, and as the most practical and efficacious method of rural segregation is discovered, these units could be gradually extended until the need of all rural areas where leprosy is a serious endemic disease has been met.

#### *Urban leprosy*

Urban leprosy is a more difficult problem than rural leprosy because of the difficulty of enforcing segregation. There are only two possible methods of urban segregation: (a) home isolation and (b) institutional isolation. If every open case would adopt the following precautions then much would be achieved in the control of the disease :—

- (a) Sleep in a separate room, taking care to sleep apart from children.
- (b) Bedding, eating and cooking utensils to be kept apart.
- (c) Personal clothing, bed clothes, towels, etc., to be soaked in antiseptic solution before washing, or preferably washed apart from the family clothes.
- (d) The patient to have his own chair or mat, and not come in close contact with children.

While it is recognized that such precautions may be difficult to maintain, yet it is to be remembered that leprosy is not solely a disease of the poor, and, therefore, if practitioners were properly instructed and health authorities sufficiently zealous, it should be possible by such means in more well-to-do areas, to accomplish a great deal towards the control of leprosy in urban districts. It cannot be too strongly stressed that just as in rural leprosy, so in urban leprosy, the disease cannot be controlled except



by segregation. Because home segregation is impossible, except for those with sufficient means, the only alternative is institutional control of all infective cases who will not or cannot isolate themselves in their own homes. Therefore, in every town where leprosy is a serious endemic disease, the municipalities, aided by Government, should actively consider the question of building a leprosy institution to care for infective cases. *There is no other way in which this problem can be solved, and the sooner this is realized, the quicker will money be forthcoming for such work, and the nearer the day when leprosy will be controlled.*

It should be said, however, that before any institution is organized a systematic investigation into leprosy in the urban area in question should be undertaken. Leprosy is not found uniformly throughout a town, but there are certain areas where there are higher incidences than others, and a survey unit should be established whose object would be to discover where the greatest concentration of cases is to be found. This means both extensive and intensive survey. Once the need for an institution is demonstrated, then the headquarters of the urban campaign should be at the institution established for the town, and the doctor in charge of the urban investigation should be actively associated with the institution, for it is a bad principle to dissociate field and survey officers completely from institutional experience and practice.

#### *General hospitals and out-patient clinics*

It has already been stressed that a person with leprosy has as much a right to receive treatment at a general hospital as a person with tuberculosis, syphilis or cancer. If the policy is accepted that all cases of leprosy suffering from acute medical or surgical conditions either due to leprosy, or to some other concomitant disease, can be admitted into a general hospital, then it would be considerably easier to develop rural centres, for if a patient in a centre needed active medical or surgical care the headquarters' hospital in the district could deal with such a situation, and it would not be necessary to overcrowd an existing leprosy institution. Similarly, while out-patient work must be part of all leprosy institutions, the fact remains that treatment should be available at all hospitals and dispensaries in a district, for again, while specialization is necessary, the ordinary general practitioner, whether in a hospital or in private work, ought to be prepared effectively to deal with cases which present themselves for treatment.

#### *Children's sanatoria*

No anti-leprosy project is likely to succeed unless the question of child leprosy is actively considered. It has been emphasized that leprosy is largely a children's disease and, therefore,

child investigation is of the utmost importance. As far as is known, the Silver Jubilee Clinic for the study of child leprosy is the only institution of its kind, and it is realized that to develop such an institution the situation must be unique, as it is in Saidapet (near Madras). It would only be profitable to consider such an institution if the number of child cases in a given area is sufficiently large, and follow-up work and repeated observation of cases is possible. Nevertheless the fact remains that the child with infective leprosy cannot be isolated under home conditions, and, therefore, the whole question of children's sanatoria for such cases must be carefully considered. These sanatoria should either be attached to existing institutions, or be specially developed—e.g. The Ettapur Children's Leprosy Sanatorium, Salem District. Whether these are separate or attached to existing institutions, they should, for all practical purposes, be separate units, with their own plans for occupational therapy, planned school curriculum, etc.

The observation of child contacts of open cases is particularly important. This would normally be done in all rural units. The doctor in charge would see that all contacts, particularly children, are examined either through periodic survey or by making special arrangements. It appears that the chief type of cases in children which need to be kept under observation is 'simple macular' leprosy and the vague hypopigmented (incipient lesion) macule which has the appearance and distribution of lepromatous leprosy but is negative to bacteriological examination.

Owing to the objection raised to the term incipient it might be better to style these lesions prelepromatous. Prelepromatous macules, we are of opinion, occasionally occur in adults but such lesions are more correctly designated 'suspicious' for no definite diagnosis can be made without cardinal signs. We have seen at least one adult with such vague lesions develop into lepromatous leprosy.

It is our opinion that most neural cases remain neural and seldom develop leproma, and that leproma arises either from the simple macule or from these so-called prelepromatous macules. We have not seen leproma ever commence as leproma. The views Dharmendra and Sen (1943) have expressed in a recent article have been ours for a long time, except that we believe that if the previous history of the cases which, he claims, start as leproma could be ascertained then it would be discovered that lepromatous leprosy is preceded by the 'prelepromatous macule'. These points are important in the control of leprosy, because it is the lack of knowledge or inability to recognize these lesions that results in these potentially lepromatous cases developing unknown to those responsible for leprosy control, and thus becoming potent sources of infection. Patients with the yet unplaced 'intermediate lesions' should generally be isolated as they are usually positive.

Any follow-up system should bear in mind the need to keep track of discharged cases. This should ordinarily be done through the district health officer and local sanitary inspector, who should be given a list of all cases discharged from institutions.

*Deformed and derelict cases*

This aspect of the leprosy problem falls under two heads:—

(a) Those who have become derelict through failure in treatment.

(b) The persons who beg because their deformities are a possible source of income.

It is recognized that even with modern methods of treatment, 60 to 85 per cent of all persons who suffer from lepromatous leprosy do not recover sufficiently for them to return to work, and the great majority of these remain infective. It may be said with regard to advanced cases that the medical profession has little appreciation of the difficulty of caring for these, particularly the advanced lepromatous patients who may be blind, badly ulcerated and crippled. These cases not only present a very difficult problem in nursing, but they usually remain infective all their days. The still commonly accepted opinion that the average life of a lepromatous case is 10 years needs to be revised. In fact it is our belief that lepromatous leprosy does not unduly shorten life, and the expectation of life is frequently almost as high as that for the country in general. If this then be the case, the time has come to consider the question of infirmaries for such cases. All institutions for the isolation of leprosy should include in their plan an infirmary section. The nursing and care of the advanced case is a constant tax on the staff of the institution. These infirmaries should be separate from the main institution, but should be an integral part of it, and special arrangements made to facilitate the nursing of such cases; a suitable staff and equipment should be provided for the care of the bed-ridden. In such infirmaries, proper bathing, cooking and toilet facilities should be available. Apart from the humanitarian side of the work, there is a great deal of investigation yet to be done in advanced leprosy. The arrangements for caring for the deformed and advanced case lag far behind the need, and no modern state should tolerate the position now seen in this country.

*Beggar problem*

The beggar with leprosy should not be specially selected for discriminate treatment. This situation can only be met by approaching the problem of mendicancy as a whole. This is largely an urban problem which has never been taken up in a comprehensive manner. As far as possible, beggars should not be treated as criminals. Where there is evidence that an individual or individuals are making their livelihood out of this unfortunate class of person, then they should be severely punished. Arrangements should be made for the care and permanent housing of all persons whose economic condition is such that they cannot maintain themselves without resource to begging. Such institutions should be staffed and managed

by a philanthropic organization which is experienced in this work. If facilities for the voluntary care of such persons are available, then all those who refuse to isolate themselves in such homes, or escape, should then be treated as trespassers against the law and be incarcerated in a prison. In these beggar homes, facilities should be given for the separation of infective cases of leprosy, but no person with leprosy who is non-infectious need be specially separated from the general class of beggars.

With regard to the person with deformity, whether he is in an establishment for beggars or in the infirmary of a leprosy sanatorium, the question of occupational therapy should be actively considered, and where persons are able-bodied and unable to be reabsorbed into society after discharge, it might be well to consider, in co-operation with the tuberculosis authorities, the question of 'after-care' colonies.

*Research*

Leprosy research to date has been confined chiefly to the School of Tropical Medicine, Calcutta, where the leprosy department has led the way in leprosy research in India and the world. As far as possible, leprosy research is carried out in Madras, but the research programme is handicapped by lack of sufficient staff and has to be pursued in conjunction with the management and direction of the several units involved in the gradual building up of a leprosy campaign. Many of the researches are undertaken in co-operation with the King Institute, Guindy, and the pathological department of the Government General Hospital, Madras. No leprosy campaign is likely to succeed unless research units with their own personnel are established, and these should work in co-operation with the proposed All-India Institute for Leprosy Research, with the leprosy departments of the teaching hospitals, the King Institute, Guindy; the Silver Jubilee Children's Clinic, Saidapet, and the Lady Willingdon Leprosy Sanatorium. Thus co-ordinated, research on a more comprehensive scale could be undertaken.

*Propaganda*

A great deal has been said about propaganda in leprosy. This actually is one of the hardest tasks, for it is very difficult in all propaganda not to give the impression that treatment is the essential measure. Propaganda material must be very carefully sifted and selected so that all publications have the same objects which are (1) to overcome the fear of leprosy; (2) to emphasize, as in tuberculosis, cancer, etc., that early diagnosis is essential; (3) to impress on the public that all leprosy is not serious; (4) to emphasize that there are three main types of leprosy from the propaganda point of view: (a) infective, (b) mutilating, (c) mild innocuous and generally abortive; (5) to stress the importance of preventing children from coming into contact with leprosy.

The public should then be taught that there is only one way to prevent leprosy and that is to insist that any case which is open or infective should not be permitted to come into close contact with children.

It should be remembered that the educated public, not forgetting the medical profession, should be the first to receive attention. Sets of lantern slides, provided they are not based on before and after treatment photographs, are very useful, and a new setting for the leprosy film more in keeping with modern ideas might be considered by the Central Government.

#### *Place of voluntary organizations in the anti-leprosy campaign*

While the control and eradication of leprosy is an inescapable duty of the Government, and nothing should be contemplated which does not emphasize this fundamental principle, the help of voluntary organizations, especially in connection with caring for the advanced and crippled cases, should not be forgotten. In this connection the pioneer work of the Mission to Lepers should be borne in mind, and wherever possible, and if mutually agreeable, their co-operation should be actively sought. As an initial step it is probably true to say that, in the first instance, in the organizing of the campaign, a medical mission's active support and help is most valuable, but unless the leprosy campaign is developed on the principle that the whole must ultimately be directed by an adequately trained and remunerated officer in Government employment, continuity is likely to be lacking, and the campaign may fail owing to insufficient official interest and support. By official interest is meant every state medical organization including the medical and health services, and the official teaching units in the province. Thus and thus only will leprosy come within the purview of all senior administrative officers. Then civil surgeons, professors of the medical colleges and central and local health officers will all combine in a united and comprehensive leprosy control system.

#### *Legal measures*

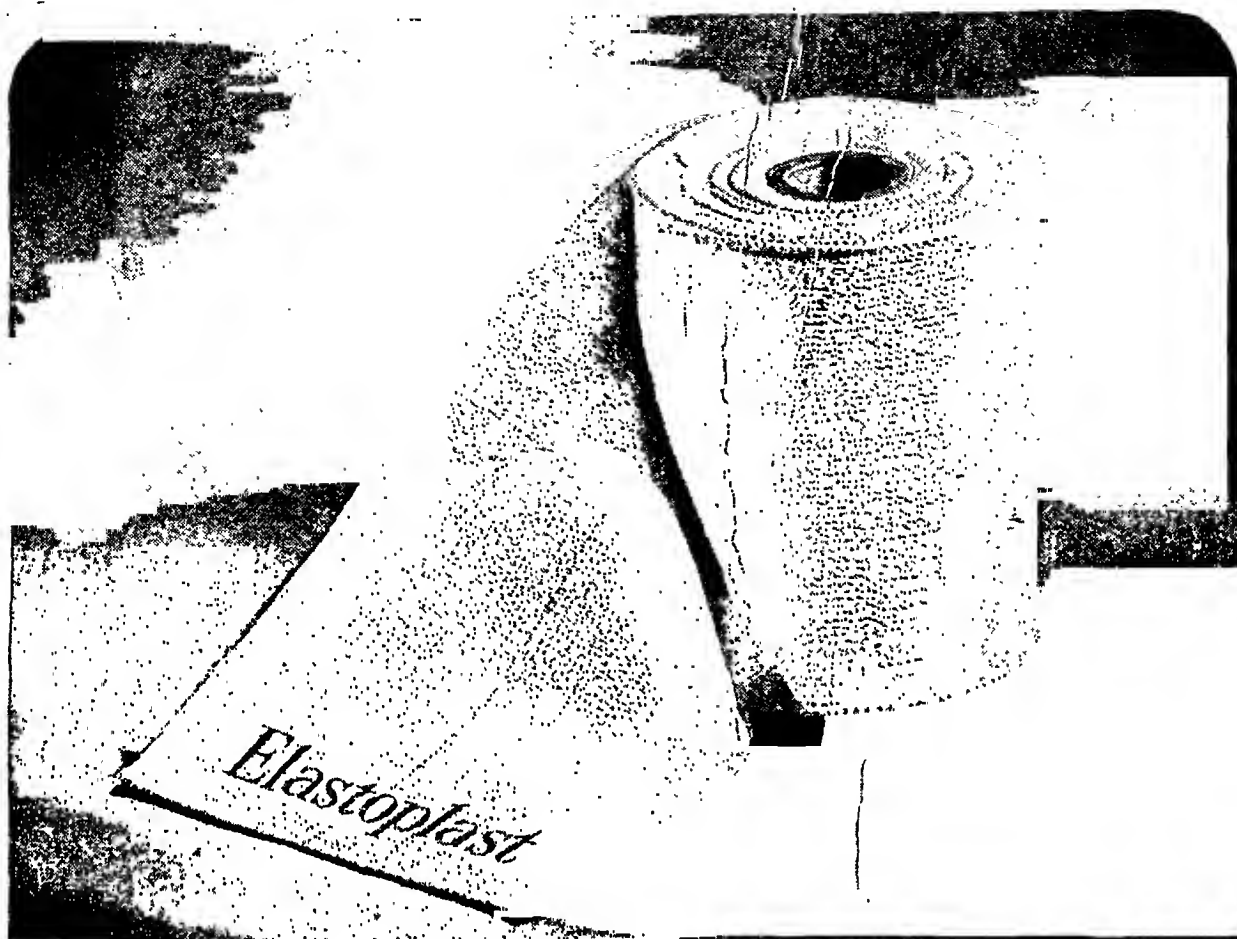
During the past two decades, there has been a great deal of controversy with regard to the matter of compulsion in the developing of anti-leprosy measures. In this connection, two fundamental principles should be borne in mind. First, any measures of compulsion which encourages concealment of the disease defeats its own purpose. Therefore, any widespread compulsory measures, unrelated either to available accommodation or to areas of high incidence of leprosy, will never succeed and cannot therefore be considered. However, some steps must be taken to compel the open case to isolate himself if he refuses to do so when provision for such isolation is available. With this end in view, the Madras Public Health Act with regard to leprosy is under modification. Leprosy in

the present Act is a notifiable disease and any one who moves in the public or exposes himself in the street can be warned by a health officer, and if he continues to mix with healthy members he can be forced into isolation. In addition, various restrictions can be imposed with regard to cases of leprosy travelling in conveyances or indulging in trades. No distinction, however, is made between open and closed leprosy. It has, therefore, been proposed that the Act be amended as far as leprosy is concerned to read :—

'A local authority may, and if so required by the Government shall, make such arrangements in its local areas as may be directed by the Government for—

- (a) the free diagnosis and treatment of persons suffering, or suspected to suffer, from leprosy.
- (b) the prevention of infection from leprosy'.

Certain occupations are prohibited to persons suffering from leprosy. In addition to the above general measures, if found necessary, provision is made for declaring any area a 'Special Area' or a 'Segregation Area'. In the former instance, regulations would be laid down prohibiting open cases from travelling in public conveyance, or in other ways coming into close contact with the public; in the latter instance, where there are facilities for segregation, such as at a leprosy rural prevention unit, persons who persistently refuse to segregate themselves and thereby are likely to jeopardize the whole scheme would be forced to isolate themselves in the segregation unit. While uncontrolled compulsory measures are bound to fail, it may be found practicable to enforce compulsory measures in local areas where there is an adequate segregation scheme. Ultimately the person who persistently refuses to come under isolation in an area where leprosy is an important endemic disease must be dealt with by methods of compulsion. This does no harm provided that (a) there are facilities for segregation and that the segregation area is near to his village, and (b) and compulsory measures are used only in cases of emergency and not applied generally. Voluntary segregation should be the main method, but where this fails it is legitimate to apply compulsion. It is hoped that as soon as the amended Act is on the Statute Book, four villages in that area which the present rural centre serves will be declared Segregation Areas within the meaning of the Act, and this will then give an opportunity of demonstrating whether a limited amount of compulsion will achieve its object. Once a method of prevention is discovered which can be applied to a rural area, this method can gradually be extended to other rural areas where it has been shown that leprosy is a serious endemic disease. The merit of the amended Act lies in the fact that prohibitive measures are only enforced where these are considered practical, and that



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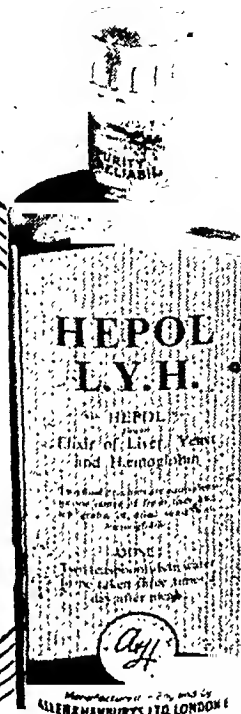
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no coercive measures are put into force except on the recommendation of the director of health who would ordinarily seek the advice of an expert on the subject.

In this connection it might be mentioned that a general rule prohibiting railway travel is not advised because this only penalizes the badly deformed and often less infective cases, whereas the better-to-do, less obvious, but often more infective case is allowed to travel without let or hindrance. The axiom that preventive measures must keep pace with facilities for segregating cases cannot be too strongly reiterated; otherwise widespread compulsory regulations without the means to enforce them will prove irksome and will hinder rather than help the development of an anti-leprosy campaign.

### Conclusion

It will be realized that in the development of such a campaign as indicated the right type of personnel is the first prerequisite. No leprosy campaign, which will of necessity take many years to organize, can be successfully pursued unless it is under the direction of an officer who will be able to control the whole development from its inception to its final completion. Therefore, provincial authorities who contemplate an adequate system of control should be prepared to appoint a medical man, young but of sufficient training, educational calibre and prestige, who will command the respect of the whole profession. This officer should have the qualifications and standing of a senior administrative health officer, and be remunerated accordingly. The first essential then is to recruit and train such an officer and place him in charge as director of the leprosy campaign. This officer should, if possible, be attached to, or be able to work in, an institution, and would also be responsible for the organization of the teaching of leprosy in the medical colleges. It is not feasible to detail the other staff necessary, such as district officers, officers in charge of survey units, etc.; these needs would arise as the campaign developed. If officers of the right type were trained to develop the campaign, and encouragement were given to medical men to take up leprosy work, it would not be long before an efficient leprosy cadre would be recruited to carry on the campaign. Once it is realized that leprosy is worthy of the attention of the best trained men, and these men are adequately remunerated, the prevailing belief that leprosy is not of sufficient interest to warrant the time of a highly qualified doctor will be dispelled. It is hoped that this contribution will assist all authorities considering schemes for post-war reconstruction, and that leprosy in the years to come will receive increasing attention, so that a problem which has baffled mankind for centuries will be tackled with determination, and the work attract the best minds of the profession. Thus, and thus only, will the prevailing apathy be dispelled, and this land

lead the way to the conquest of a disease which, if not of great economic importance, yet results in more misery to the lives and souls of men than almost any other disease known to mankind.

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The Report of the International Congress of Leprosy (Cairo, 1938) defines the following terms:—

- (1) The gross incidence of leprosy is the number of cases of leprosy per thousand of the total population.
- (2) The child rate is the number of child cases per hundred cases of leprosy.
- (3) The open case rate is the number of open cases per hundred cases of leprosy.

## Current Topics

### Dry Blood Test for Typhus Fever

By P. N. BARDHAN, M.R.C.P. (Edin.)

MAJOR, I.A.M.C.

N. TYAGI, I.A.M.C.

and

K. BOUTROS

LIEUTENANT, R.A.M.C.

(From the *British Medical Journal*, i, 19th February, 1944, p. 253)

IN 1942 Steuer utilized a slide-agglutination method for the rapid diagnosis of typhus fever. He claimed that 200 slides could be examined in 90 minutes, and that each individual slide could be read in from 5 to 10 minutes. We found his technique unnecessarily cumbersome, and it was therefore modified by us to make it more workable for general use. The essential difference between the two techniques was that, while Steuer used *exactly* measured quantities of blood and antigen suspension, we used *approximate* quantities. The technique we employ is:

### METHOD

Place on a clean glass slide two drops of blood, obtained by pricking the finger or the ear lobe without squeezing, separated from each other by a grease-pencil line. Dry in air and mark the drops 1 and 2. Place a drop of concentrated suspension of OX 2 and OX 19 on blood drops 1 and 2 respectively. Leave for a minute, and then complete the mixing of the blood and the suspension by gently rocking the slide. (Mixing with a platinum loop or other foreign object tends to produce strings of fibrin, which cause confusion in reading the results.) Set aside for 5 minutes; taking



care to avoid drying up of the slide and soiling by dust. Rock the slide occasionally.

Results are read in from 5 to 10 minutes by the naked eye, and if necessary are confirmed by a hand-lens. The use of the low-power objective, as recommended by Steuer, is rarely necessary.

#### RESULTS

The tests were carried out on Egyptian labourers. Slides were taken in various camps under military control, were brought to the laboratory the same day, and were examined within the next 24 hours. In all, 640 persons were examined; 11 of these gave 'slide-positive' results against OX 19, and 2 were positive to OX 2 in addition. These 13 were then followed up for a complete Weil-Felix reaction, using Dreyer's technique. The results are summarized in table I.

TABLE I

Positive to OX 19 ..	..	..	7*
Negative to OX 19 ..	..	..	6

\* Of these 7 positives, 2 also showed agglutination in 1/50 against OX 2; and these 2 were the same persons who were slide-positive for OX 19 and OX 2.

The 7 'slide- and Dreyer-positive' cases were further studied by carrying out a series of Weil-Felix tests at 4-day to 7-day intervals. The results obtained are shown in table II.

TABLE II

Serial number		1st test	2nd test	3rd test	4th test	REMARKS
3	OX 2	0	50	..	..	Had typhus a month before first test.
	OX 19	250	250	..	..	
4	OX 2	50	50	50	..	Not traceable afterwards.
	OX 19	50	125	500	..	
12	OX 2	50	..	..	..	Had typhus 3 weeks previously in hospital.
	OX 19	500	..	..	..	
19	OX 2	0	..	..	..	Not traceable: history not available.
	OX 19	500	..	..	..	
20	OX 2	0	0	..	..	Hospital ease: diagnosed typhus.
	OX 19	1,280	2,560	..	..	
21	OX 2	0	0	..	..	Typhus with rash.
	OX 19	250	1,800	..	..	
22	OX 2	0	0	0	0	Typhus with rash.
	OX 19	250	250	1,250	1,250	

Nos. 4 and 19, despite of the history being unobtainable, should be considered typhus cases in view of the high titre. The others were definite typhus cases. It will thus be seen that all the clinical and Weil-Felix-positive typhus cases showed 'slide agglutination' as well.

The results of the 6 slide-positive and Dreyer-negative cases (see table I) are detailed in table III.

TABLE III

Serial number	1	2	7	13*	15	17
OX 2 ..	0	0	0	0 0	0	25
OX 19 ..	0	0	0	0 0	50	50

\* Done twice, at five-day interval.

Except in 2 cases, there was no agglutination by Dreyer's method, and in neither of these was the titre

high enough for diagnosis. These observations suggest that negative cases may occasionally give positive results, but this is not of much import. The fact that every clinical typhus case which was proved positive by the Weil-Felix reaction was spotted by the slide method is justification enough for urging the use of this simple technique as a preliminary to putting up a long series of tests by Dreyer's or Felix's method.

It was decided to try out a number of slide-negative cases by Dreyer's method, to see whether the zone phenomenon or some other factor would produce positive results in slide-negative cases. Thirty-three such sera were tested; the highest dilution put up was 1 in 250 and the lowest 1 in 25. Of these, 25 were completely negative; the remaining 8 gave agglutinations as shown in table IV.

TABLE IV

Serial number	25	27	29	32	35	45	50	52
OX 2 ..	0	25	0	50	25	25	0	25
OX 19 ..	25	0	25	0	25	0	25	0

None of these titres has any diagnostic value.

It is reasonable to conclude from these results that a slide-negative blood will not give a positive Dreyer reaction—certainly not of any diagnostic value. The low titres given in table IV have no significance beyond perhaps the possibility that the individuals had developed some immunity as a result of subclinical infection, or had suffered from the disease some time previously.

#### COMMENT

Having established that all positive cases can be detected by the slide method (of course to be confirmed by a complete agglutination test), and that the slide-negative cases will not give a positive result by Dreyer's method, it is a reasonable assumption that a complete Weil-Felix test need not be done unless the slide test is positive. If this procedure is followed the obvious advantages will be: (a) economy in material and time; (b) avoidance of unnecessary bleeding of the patient; and (c) easier despatch of slides, as compared with that of blood or serum, to a laboratory situated at a distance from the hospital. Probably the test could be done on thick smears of blood, similar



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to those used for the detection of malaria parasites, and taken at the same time.

#### SUMMARY.

A dry blood test for typhus has been tried out among Egyptian civilians.

It has been shown that all typhus cases give a slide-positive result, though a slide-positive result does not necessarily mean a positive case.

Control tests show that a negative slide will not give a positive Weil-Felix reaction.

The need for trying out this method on a more extensive scale is urged, and the advantages to be derived therefrom are discussed.

### More Light on the B Complex

(From the *British Medical Journal*, i, 15th January, p. 85)

IN 1940 Van Etten and others found that the administration of an ample supply of crystalline vitamin B<sub>1</sub> did not prevent convulsions and nerve degeneration in swine fed on autoclaved liver and whey. The experiments of Wintrobe carry the matter a stage further, with an accurate description of symptomatology and pathology in pigs receiving all the known members of the B complex except B<sub>1</sub>. The earliest clinical manifestations were failure of appetite and vomiting, followed by cyanosis, dyspnoea, and bradycardia, and ending with a severe degree of heart failure or sudden death. No abnormality of neuromuscular disturbance, such as ataxic gait, was ever observed. Careful histological examination of the nerve tissues, central and peripheral, gave no evidence of degeneration or inflammation, but in practically every case local necroses of the myocardial fibres were present in both auricles and ventricles. Where the pathological condition had not advanced too far, administration of B<sub>1</sub> led to recovery. Of particular interest are the biochemical findings. The concentration of carbonyl compounds estimated as pyruvic acid was proportional to the degree of severity of the deficiency as judged by the clinical manifestations. A sharp rise in blood pyruvic acid was quickly followed by the rapid progress of the disease. It was also found that a significant increase in blood pyruvic acid after the administration of glucose always occurred in B<sub>1</sub>-deficient animals but not in the control group. As for urinary content of B<sub>1</sub>, it reflected—but by no means consistently—the dietary intake immediately before the collection of urine. Of more value in assessing the degree of B<sub>1</sub> deficiency was the percentage retention of B<sub>1</sub> after a given dose. This test, suggested by Najjar and Holt, gave results which can parallel with the clinical findings and the amount of B<sub>1</sub> in the diet.

It is clear from this work that the position of vitamin B<sub>1</sub> as the antineuritic vitamin has been strongly assailed, supporting the sceptical view put forward by Meiklejohn in 1940. He concluded his review with the statement that probably a multiple deficiency is responsible for nutritional neuritis but that there is still a possibility that the true antineuritic vitamin has yet to be discovered. By the use of crystalline vitamins Wintrobe and his colleagues have shown that neither riboflavin nor nicotinic acid has any effect in maintaining the integrity of nervous tissue. It was then found that the ataxic gait and the degenerative nerve lesions brought about by a dietary deficiency of the vitamin-B complex are completely prevented by whole desiccated liver. The anti-pernicious-anæmia fraction was found to be the most potent of the individual liver fractions, none of which are as efficacious as whole liver, even when given parenterally, and the results suggest that there is a need for passage of the nerve-protection factor through the gastrointestinal tract. Finally, it has been shown that the dietary deficiency of either pyridoxine or pantothenic acid leads to an ataxic gait in swine and degeneration of sensory neurones which could invariably be prevented by the administration of these substances. The claim

of one of these constituents of the vitamin-B complex is considerably strengthened by the finding that the protective actions of the various liver fractions is proportional to their contents of pantothenic acid.

### Despeciated Bovine Serum (D.B.S.): A Substitute for Human Plasma

By F. R. EDWARDS, M.D., CH.M., F.R.C.S.

(Abstracted from the *British Medical Journal*, i, 15th January, 1944, p. 73)

SUBSTITUTES for human plasma hitherto prepared have not fulfilled the three criteria: (a) retention in the circulation and eventual metabolism; (b) exertion of an equivalent osmotic pressure; and (c) non-toxicity non-antigenicity, and freedom from antibodies.

Bovine serum can be made safe for man by destroying the antibodies by heating to 72°C., while rendering the proteins uncoagulable with the addition of 0.2 per cent of formalin and ammonia. Material so prepared appears to accord with the above precepts.

Clinical trial in 26 cases shows that it can be administered rapidly and in large amounts to man with safety.

### A New Typhoid Vaccine for the Army

(From the *Lancet*, i, 4th March, 1944, p. 318)

THE British Army authorities have decided to change the well-tried T.A.B. vaccine, which was heat-killed and preserved in carbol-saline, for a new preparation which is killed by 75 per cent alcohol and preserved in 25 per cent alcohol. As before, great importance is attached to the use of fully virulent strains and the vaccine contains the full complement of Vi antigen which is so important in producing a high level of protection. Several points about the new alcoholized vaccine should be kept in mind. Bacteria suspended in alcohol sediment more completely than in saline, and unless the bottle is thoroughly shaken the bacteria sit tight and the syringe may not withdraw the proper dose of organisms. The doses of the new vaccine are smaller than those previously used. For men 0.25 c.c.m. is followed after at least a fortnight by 0.5 c.c.m., while for women the doses are 0.2 c.c.m. and 0.4 c.c.m. Annual reinoculation with 0.25 c.c.m. is recommended for both. There was doubt at one time about the ability of 25 per cent alcohol to effect sterility if the vaccine became contaminated during use, but this fear has been proved groundless. The chief advantage of the new vaccine is that alcohol preserves the integrity of the Vi antigen, as Felix has shown, and it also probably induces a superior antibody response. Both local and general reactions are less severe than with the old vaccine; Felix, Rainsford and Stokes and workers of the Emergency Public Health Laboratory Service, point out that the average time lost through reaction by those receiving TABO vaccine is likely to be considerably less with an alcoholized than with a phenolized product. Even so, the new vaccine produces an initial stinging pain on injection and some people still get a local reaction and a slight rise of temperature. In future it may be possible to produce even more inoffensive TAB vaccines. The question of adding a representative of the *paratyphosum* C group of organisms was considered, but infections of this kind in the Army were so few that this procedure was not adopted. Meanwhile there are sound reasons for the resignation of TAB from the active list and for the seconding of TAB Alc. to take its place.

### The Uses and Abuses of the Female Sex Hormones

By T. N. MACGREGOR, M.D., F.R.C.S.E.D., M.R.C.O.G.

(Abstracted from the *Edinburgh Medical Journal*, Vol. LI, January, p. 39)

THE hormones most closely related to female sex physiology are the gonadotrophic hormone secreted by

the anterior pituitary gland, oestradiol elaborated by the developing Graafian follicles of the ovary, and progesterone secreted by the corpus luteum.

#### ANTERIOR PITUITARY GONADOTROPHIC HORMONE

The anterior pituitary gland through its gonadotrophic hormone controls the development of the Graafian follicle, ovulation and corpus luteum formation. At the present time there is no reliable anterior pituitary preparation available for use which can simulate the actions of the naturally occurring gonadotrophic hormone; there are, however, two preparations which are of considerable therapeutic value, namely, serum gonadotrophic hormone prepared from pregnant mare's serum, and urine or chorionic gonadotrophic hormone extracted from pregnancy urine. The former stimulates follicular development; the latter causes corpus luteum formation. A combination of these two preparations forms a useful therapeutic agent indicated in conditions directly or indirectly associated with defective action of the anterior pituitary gland.

#### THE OVARIAN HORMONES

The ovarian hormones are oestradiol or oestrogenic hormone elaborated by the developing Graafian follicles, and progesterone secreted by the corpus luteum not only elaborates its specific hormone, progesterone, but it also secretes oestradiol. Progesterone and oestradiol are the true or naturally occurring hormones of the ovaries and are produced for the most part by the ovaries under the stimulus of the gonadotrophic hormone of the anterior pituitary; they are also secreted in variable amounts by other internal secretory glands, such as the adrenals. Potent preparations of these hormones have been available for some time. Now we have available for clinical use synthetic preparations of oestrogenic hormone, such as diethyl stilboestrol, hexoestrol and triphenylchloroethylene which, though not chemically related, simulate closely the actions of the naturally occurring hormones. They have the added advantage of being active when given orally.

Anhydro-oxy-progesterone is a synthetic preparation of progesterone which is also active when given by mouth, but the effective dosage given orally is six times that given by injection.

The uses of the sex hormones may conveniently be considered in two groups: gynaecological disorders and obstetrical conditions.

#### GYNÆCOLOGICAL DISORDERS

##### (A) BEFORE PUBERTY

As the sex glands only assume full function at puberty, there are thus few indications for the use of the sex hormones before this time. There is one condition, however, namely, vulvo-vaginitis, which can be effectively treated by oestrogenic hormone in the form of vaginal pessaries or by oral administration. The oestrogens stimulate the growth of the vaginal epithelium, and with the resulting increased glycogen content of the cells additional lactic acid is available so that not only is the infection controlled by the shedding of the epithelial squames, but the increased acidity of the vaginal flora proves inimical to the causative organism.

It should be noted that the sulphonamides, especially sulphathiazol and sulphadiazine, are also effective in this condition and have none of the minor disadvantages, such as enlargement of the breasts, which are sometimes associated with the administration of the oestrogens.

##### (B) DURING THE PERIOD OF REPRODUCTIVE LIFE

###### (1) Disturbances of menstrual rhythm

(a) *Metropathia hæmorrhagica*.—The most common cause of irregular uterine bleeding is metropathia hæmorrhagica or cystic glandular hyperplasia. This condition may occur at any time, but is more common at the beginning and end of the period of reproductive

life. It is characterized by a long intermenstrual period, five to ten weeks, followed by excessive and prolonged menstrual loss. It is possible that a minor psychological disturbance, acting through the higher cerebral centres and interfering with anterior pituitary function, forms the predominant etiological factor in metropathia hæmorrhagica. The essential cause of the condition, however, is a failure of ovulation with concomitant excessive production of the oestrogenic hormone.

In the present state of our knowledge progesterone seems to be the most effective therapy for metropathia hæmorrhagica and, pending more potent anterior pituitary preparations, it is the one most likely to meet with success, but the dosage must be adequate and the treatment must be energetic if satisfactory results are to be obtained. The intramuscular injection of 5 to 10 mg. of progesterone daily until the bleeding is controlled has been found to be an effective dosage.

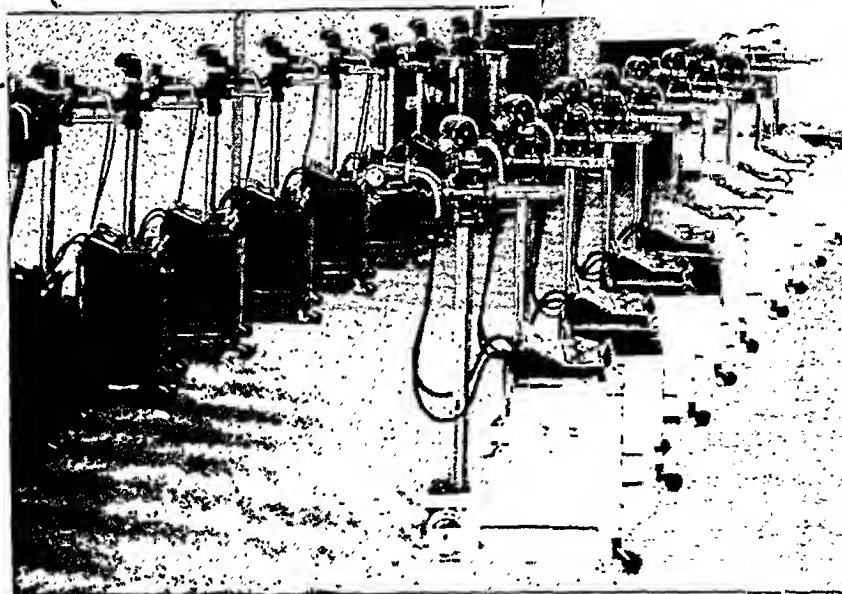
The rôle of the oestrogenic hormone in functional uterine bleeding has recently been investigated, and not unfavourable results have been reported. The results obtained in cases of irregular uterine bleeding treated by oestrogenic hormone, and later referred to me, have been uniformly unsatisfactory.

(b) *Ovular bleeding, hypomenorrhœa and oligomenorrhœa*.—These are minor disturbances of the menstrual rhythm. Ovular bleeding, as the term implies, is the bleeding which is sometimes associated with ovulation. It is believed to be due to a transient diminution of the oestrogenic hormone concentration occurring between the time of ovulation and mobilization of the corpus luteum. The temporary drop in the amount of circulating oestrogenic hormone results in a diminished stimulation of the uterine endometrium, which partially breaks down and causes bleeding. In some the bleeding may be very slight and represented by only a few spots, whilst in others the amount of blood lost may be similar to that of the normal period. Owing to the danger of inhibiting directly the anterior pituitary and indirectly ovulation, oestrogenic hormone is contra-indicated in this condition. The stimulation of the endometrium can, however, be adequately maintained in such cases by giving 5 mg. progesterone intramuscularly the day before the expected bleeding and for two days thereafter. A course of therapy over three menstrual cycles is usually efficacious.

Hypomenorrhœa, or scanty menstrual loss, is not common and in most cases it is of no serious significance, as in such cases there is usually no failure of ovulation. There are a few cases, nevertheless, in which there is failure of ovulation, and in such the bleeding is associated with the proliferative phase of the endometrium—so-called anovular menstruation. The importance of this type of menstruation in sterility is evident. An effective therapy must promote follicular maturation and ovulation; this can only be done by administration of anterior pituitary hormone, particularly the serum gonadotrophic hormone, given in doses of 200 international units every third day for five injections, starting at the onset of the menstrual period.

Oligomenorrhœa, or delayed menstruation, is not uncommon. It is a frequent precursor of functional amenorrhœa and is prone to occur at the beginning and end of the period of reproductive life. Towards the menopause the bleeding is frequently associated with a proliferative endometrium, but at other times for the most part it is associated with a secretory endometrium. Thus there is a long proliferative phase of the endometrium and a normal secretory phase. The therapy indicated is one which will accelerate follicular development and ovulation; accordingly, the treatment most likely to be effective is the administration of anterior pituitary in the form of serum gonadotrophic hormone (200 i.u.) alone or in combination with urine gonadotrophic hormone (100 i.u.) every third day for five injections at the onset of the period. These preparations should be given over three menstrual cycles at the time corresponding to the pre-ovulatory phase.

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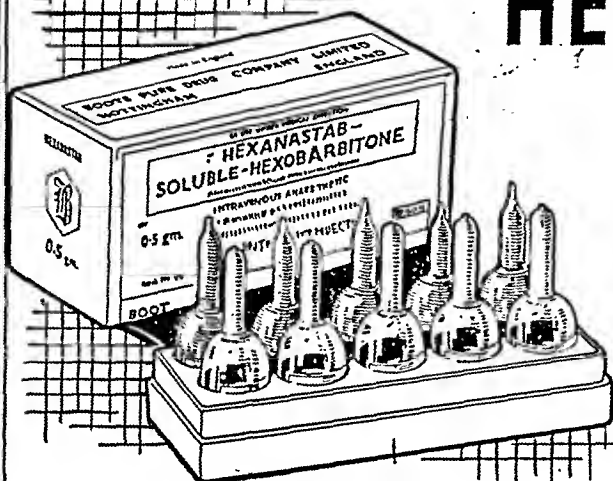


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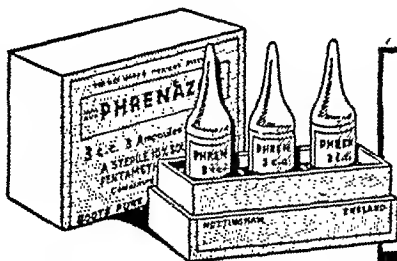
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(2) *Dysmenorrhœa*

There are many cases, in which no obvious pathology exists and, although there may be a psychological basis for the pain, hormone therapy is frequently efficacious. It is reasonable to assume that the rhythmic interplay of the ovarian secretions, which exert their influence on the uterus and uterine adnexa, may be maladjusted and increased function of one partially override the function of the other. It is known that the oestrogenic hormone sensitizes the uterine musculature, promotes the proliferative phase of the endometrium and increases the vascularity of the pelvic structures; whereas progesterone inhibits uterine activity and stimulates the secretory phase of the endometrium. The important point to keep in mind, however, is that the corpus luteum secretes both hormones and that they act synergistically on the uterus. Primary dysmenorrhœa, in my experience, is invariably associated with ovulation; women who do not ovulate do not have painful periods. This is clearly demonstrated in cases of ovular bleeding, œstrin-withdrawal bleeding and the bleeding associated with metropathia hæmorrhagica. In this case there is unopposed oestrogenic action, and consequently there is no pain associated with the bleeding. Painful menstruation is not necessarily associated with uterine hypoplasia or hyperplasia *per se*.

As a result of clinical investigation, one believes that it is only when there is a deviation from the normal finely adjusted concentration of the two ovarian hormones that the uterine reactivity becomes disordered, giving rise to pain either before or during menstruation. If this contention is correct, then hormone therapy for the relief of dysmenorrhœa should only be given during the second half of the menstrual cycle. Premenstrual dysmenorrhœa, in the absence of pelvic pathology, is most frequently associated with excessive oestrogen or deficient progesterone production, and can be controlled by progesterone therapy in doses of 5 mg. every second day, starting eight days before the expected period. Conversely menstrual dysmenorrhœa may be associated with excessive progesterone or subnormal oestrogenic hormone secretion, and can be relieved by the administration of oestrogenic hormone in doses of 5 mg. of synthetic preparation given thrice daily for four days prior to the onset of the period. The oestrogenic hormone is frequently administered during the first half of the menstrual cycle in cases of dysmenorrhœa, and this form of therapy may be temporarily effective, but it acts by suppressing ovulation and consequently there is always the danger of producing an abnormal condition, the treatment of which may be much more difficult than that of the primary disturbance.

(3) *Sterility*

It is important to understand the rôle of the female sex hormones in the treatment of sterility, as they are frequently misused in this condition. Now, if ovulation takes place, corpus luteum formation follows normally—this is confirmed if one obtains a typical secretory endometrial pattern in the tissue removed with the biopsy curette immediately before a period, or if pregnandiol can be recovered from the urine in the post-ovulatory phase—and there would therefore appear to be an indication for hormone therapy. If repeated examinations—and one examination is not conclusive—show that ovulation is not occurring, then an anterior pituitary preparation to stimulate ovulation is indicated. It has been shown that anterior pituitary preparations, especially serum gonadotrophic hormone, can promote ovulation. Green-Armytage contends that small doses of oestrogen, for example,  $\frac{1}{2}$  to 1 mg. hexœstrol, given daily during the first five days of the cycle, that is during menstruation, have a beneficial effect not only on the pH of the vaginal secretion, but also promote a healthier condition of the mucous plug—conditions favourable to the spermatozoa. There is also convincing evidence that administration of the oestrogens promotes canalization of the Fallopian tubes in proved cases of tubal occlusion. These causes

of sterility are found only after thorough investigation, and the oestrogens are given in order to evoke a definite and known response. The danger of oestrogenic therapy in sterility, however, is that of so depressing pituitary function as to inhibit ovulation, thus preventing the occurrence of conception and promoting a pregnancy complex.

(4) *Amenorrhœa*

Although amenorrhœa is due in most cases to a physiological or a pathological condition, there is, nevertheless, a large number of cases in which no cause for the amenorrhœa is apparent. A study of the history in such cases, however, leads one to the conclusion that in the majority there is an exciting psychological disturbance; in some it is trivial, whilst in others it may be grave.

When potent preparations of the ovarian hormones became available the outlook in the treatment of amenorrhœa appeared promising, but the results obtained have not fulfilled the earlier expectations of this form of therapy.

(5) *The menopause*

An important factor in the production of an unfavourable mental reaction is the fear of loss of sexual function—many women believe that sexual life ceases at the menopause—and the allaying of this dread may frequently change the whole outlook.

There appears to be no indication for the use of the oestrogens in irregular bleeding occurring at the menopause, for the reason that the bleeding may be associated with an already excessive secretion of the hormone and any effect can only be of a very temporary nature. It should be emphasized that slight irregular uterine bleeding in women at the menopause may be symptomatic of a pathological process, and the administration of oestrogenic hormone in these cases, though it may temporarily arrest the hæmorrhage, merely masks the serious condition and delays, not without danger, operative or other appropriate treatment. It is astonishing, however, how frequently the oestrogens are abused in the treatment of women complaining of menstrual irregularities at the climacteric.

The oestrogens are pre-eminently effective in controlling the subjective symptoms associated with the cessation of ovarian function. The hot flushes, irritability, depression, etc., which are so common and which, as already pointed out, are conditioned to a certain extent by the psychological status of the individual, can be completely relieved by oestrogenic hormone therapy. For this reason a high dosage of the oestrogens, such as 5 mg. synthetic oestrogen thrice daily, should be given until all symptoms are relieved, and then the dosage should be gradually diminished over a period of six to eight weeks. Satisfactory results have been obtained in the artificially induced menopause by the administration of small doses of the oestrogens given as a prophylactic measure before any untoward symptoms arise.

It is important to recognize that occasionally the menopausal phase may pass imperceptibly into the abnormal and that some patients, complaining initially of mild depression, may become definitely psychotic. The oestrogens are of value in such cases when used as an adjuvant to general psychiatric treatment.

(C) *POST-MENOPAUSE*

In cases of senile vaginitis and kraurosis vulvæ the restoration of the tissues, by the administration of oestrogenic hormone, to the same state of development as that found during reproductive life, supplies the necessary resistance to overcome the infection. There is increased vascularity of the tissues and regeneration of the epithelium, and, in senile vaginitis, the change in the vaginal flora makes it inimical to the causative organism. Leucoplakia vulvæ, if treated in the early phase, responds satisfactorily to this treatment but may prove refractory in the later stages. The dosage of the oestrogens employed in these conditions should be a large one, say 15 mg. daily, administered over a short period.

The administration of the oestrogens to elderly women subsequent to operation for genital prolapse promotes the vascularity and regeneration of the tissues, which ensure sound healing. This therapy proves particularly beneficial in those cases in which the vaginal tissues are unduly friable and atrophic.

Pruritis vulvæ is not uncommon after the menopause, and in the majority of cases a specific etiological factor can be ascertained. There are some cases, however, in which no cause can be found, and in these the condition may be associated with some irritative lesion of the nerve endings arising from the atrophy of the tissues. Oestrogenic hormone therapy is often eminently successful in these resistant and difficult cases. It may be necessary to give a very high dosage if no result is obtained with a moderate dose. It should be noted, however, that it is not advisable to give a high dosage over more than a short interval of time. One case treated did not react favourably until a dosage of 45 mg. of synthetic oestrogen was given daily for seven days. The pruritis was completely relieved. This high dosage of oestrogen, however, provoked such a marked hypertrophy of the vaginal epithelium as to form a plaque in the anterior wall. Cystoscopic examination suggested a malignant condition of the base of the bladder, but the vaginal mucosa eventually returned to its normal post-menopausal state. The patient remained free of irritation until a recurrence two weeks ago.

The most common etiological factor responsible for post-menopausal bleeding is a malignant condition of the uterus or its adnexa. It cannot be emphasized too strongly that post-menopausal bleeding; *per se*, is never an indication for oestrogenic hormone therapy, yet one frequently finds it being given quite unjustifiably in this condition.

Some women may have an uneventful climacteric but complain of subjective symptoms late in life similar to those experienced at the menopause. Such cases can be effectively treated with the oestrogens, but they usually require a small maintenance dose given over a prolonged period.

#### OBSTETRICAL CONDITIONS

The corpus luteum hormone or progesterone has well-defined physiological actions in the initiation and continuation of pregnancy. It is responsible for the decidual reaction of the uterine endometrium, thus preparing the endometrium for the nidation of the fertilized ovum. Its sedative action on the uterine musculature promotes conditions favourable for the process of embedding of the ovum and the early development of the placenta, and its uninterrupted production is essential for the continuation of the pregnancy. Consideration of these facts suggests the usefulness of progesterone therapy in (1) repeated early miscarriage suspected when the period is a few days late, (2) threatened abortion, and (3) recurrent abortion.

(1) *Early miscarriage*.—This frequently occurs without the patient's knowledge, or it may be suspected when the period is repeatedly but not continuously a few days late. Some women realize intuitively that conception has occurred. A continuation of the pregnancy in such cases can be brought about by the administration of progesterone, 5 to 10 mg. twice weekly, begun during the second half of the menstrual cycle and continued until at least the fourth month is reached.

(2) *Threatened abortion*.—Abortion most frequently occurs at the time of the suppressed period, and it reaches its highest incidence at the time of the third missed period. The explanation for the frequency of abortion at the third month is not clear. The placenta, by the time this stage is reached, is fully developed. It is known that pregnancy can continue when the corpus luteum of pregnancy is removed at an early stage. The assumption is, therefore, that the placenta secretes the necessary amount of progesterone required for the continuation of the pregnancy. The change over from corpus luteum to placental production of

progesterone probably takes place at the third month. A lag in the change over, resulting in a lowering of the progesterone threshold, would furnish an explanation of the frequency of abortion at this time. The administration of progesterone in large doses (10 to 20 mg. daily) at the very earliest stage of a threatened miscarriage is frequently effective in saving the pregnancy. If much placental separation has occurred, however, the abortion will become inevitable and progesterone therapy is then valueless. It should be noted that progesterone therapy alone in threatened miscarriage is not enough; rest must be enforced and anxiety allayed by the use of sedatives.

(3) *Recurrent abortion*.—The administration of progesterone early in pregnancy has resulted in the continuation of the pregnancy to term in many cases of recurrent abortion. An adequate dosage, such as 5 to 10 mg. twice weekly, must be given as soon as the pregnancy is diagnosed and continued until at least the end of the fourth month of pregnancy. It is advisable to supplement this therapy by the administration of vitamin E.

The oestrogens, in virtue of their function of increasing the sensitivity of the uterine muscle, have been used in (a) missed abortion, (b) induction of labour, and (c) uterine inertia.

(a) *Missed abortion*.—As is well known, a dead ovum may be retained *in utero* for intervals of time varying from weeks to months. The cause of the retention of the ovum is presumably the diminished sensitivity of the uterine muscle. This can be overcome by the administration of oestrogens, and this form of therapy is frequently very successful in missed abortion and premature death of the foetus. As the oestrogens are fairly rapidly destroyed in the body, it is suggested that a high dosage should be given over a short interval of time. I have obtained satisfactory results with 10 mg. of synthetic oestrogen given hourly for six to ten hours, supplemented in some cases by posterior pituitary extract. This high dosage is well tolerated. The more advanced the pregnancy the more successful is this form of treatment.

(b) *Induction of labour and premature death of foetus*.—When giving alone the oestrogens are rarely effective in inducing labour but when employed as part of a scheme of induction they may be of value, although their usefulness in these cases is difficult to assess. They are, however, efficacious in the induction of labour in cases where the foetus dies *in utero* near term, and also in some cases of premature rupture of the membranes associated with delay in the onset of labour.

(c) *Uterine inertia*.—The oestrogens have been found to be effective in more than half of a series of cases of uterine inertia. In my experience the results of this form of therapy have been inconclusive, as it has not been found possible to induce increased uterine sensitivity in many cases in which the indications for its use appeared to be specific and in which a satisfactory response was anticipated.

#### SUPPRESSION OF LACTATION

The development of the breasts during pregnancy in preparation for lactation is brought about by the actions of the oestrogenic and corpus luteum hormone.

The secretion of milk in the breasts on the third or fourth day of the puerperium is due to prolactin or mammatrophic hormone of the anterior pituitary gland, whilst the continuation of milk production is associated with the stimuli arising from the act of suckling. During pregnancy and for the first two or three days of the puerperium the mammatrophic hormone of the anterior pituitary is probably inhibited by the high blood concentration of the oestrogenic hormone; the delivery of the placenta results in the release of this inhibition. The administration of oestrogens, however, either before or after lactation is established, can again bring about the inhibition of the anterior pituitary milk secreting hormone; the breast either does not secrete milk or its secretion quickly subsides with this therapy, provided suckling

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emerged as 'the most effective stimulant.' Briefly, it was proved that Bovril increased the supply of gastric juices where there was a deficiency and restored it to normal. It is an accepted medical fact that people of sedentary habits generally suffer from a lowering of the essential gastric activity; Bovril rectifies this and, by facilitating the digestion of proteins, enables full nourishment to be gained.

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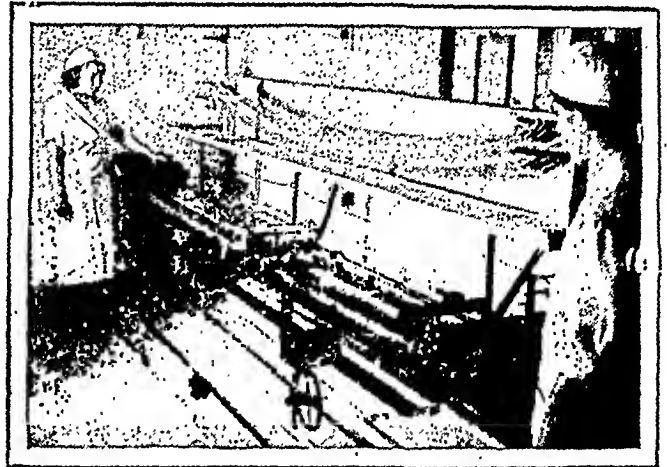
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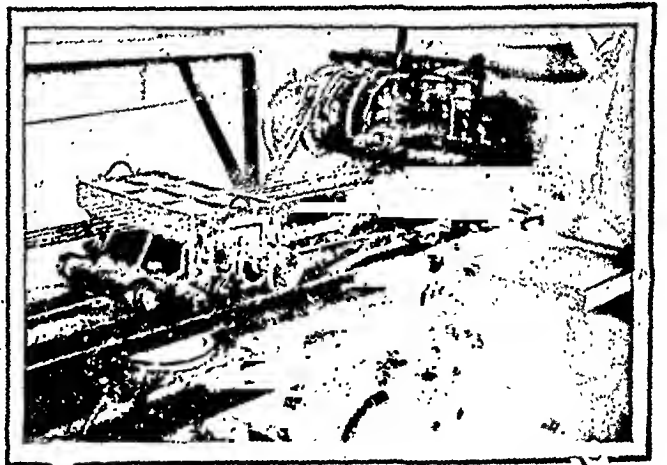
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does not take place. As the administration of oestrogens to a nursing mother does not inhibit the secretion of milk, it would seem that the reflex act of suckling must stimulate the increased secretion of prolactin. The important part played by the act of suckling in hormone production, leading to milk secretion, suggests how readily the endocrine system is influenced by nervous stimuli.

In cases where breast feeding is contra-indicated, oestrogen therapy should be started the day after delivery. It is advisable to give an effective dose initially—5 mg. thrice daily for four days, followed by 5 mg. daily for six days is usually effective—in order to produce complete inhibition of the lactogenic hormone. Lactation can be inhibited in every case provided the dosage is adequate; the puerperal patient can tolerate a high dosage of oestrogenic hormone.

The chemist has provided us with potent preparations, and it behoves us as clinicians to realize that the indications for their use must be defined and limited, and that their misuse may be fraught with serious consequences. Intelligently and wisely used, they can be of inestimable value.

## Reviews

**FRACTURES AND JOINT INJURIES.**—By R. Watson-Jones, B.Sc., M.Ch. Orth., F.R.C.S. (L'pool). Volumes I and II. Third Edition. 1944. E. and S. Livingstone, Edinburgh. Pp. xi plus 407 in volume I and pp. vii plus from 408 to 960 in volume II. Illustrated. Price 75s. Postage 1s.

To those who have read the first edition of Mr. Watson-Jones' 'Fractures and Joint Injuries', it will not come as a surprise to learn that a third edition is now on the market within three years. This new edition in two volumes contains much new material and many fresh illustrations, both photographic and coloured. Two hundred pages of new material have been added and the new edition contains one of the most perfect collections of illustrations in any medical or surgical textbook.

Every phase of repair, every complication and every method of treatment is so well illustrated that the reader in a hurry can gain a very fair idea of the subject from a study of the illustrations and legends alone. Mr. Watson-Jones has been at great pains to make the pictures teach, and several devices have been incorporated to drive home his points. Many of the illustrations are set beside a twin picture covered by a flap. The reader is asked to draw his conclusions from the photograph on view and then compare it with that covered by the flap which illustrates the same fracture viewed from a different angle, taken with the joint in a different position or taken a few weeks after the first. The lessons are frequently striking and impressive.

In one section he goes the length of a cut-out model which can be fitted to the picture, in the text to illustrate the degree of plantar flexion necessary to reduce a fractured neck of the talus. The text also is easy to read and occasionally streaked with sly humour and, what is particularly refreshing, frequent references to the careers and contributions of the great men of the Liverpool School and particularly to many of Mr. Watson-Jones' contemporaries and juniors.

A pleasing feature of the methods described is the simplicity of the apparatus required. Armed with plaster of paris, adhesive strapping and Thomas splints one can carry out three-quarters of the procedures required for reduction and fixation. Few surgeons in the forward area in war or in a cottage hospital in the country are without the wherewithal to obtain excellent results provided they give time and care to study the problem on hand and understand the principles so well set out in this book. More elaborate apparatus

is described and no doubt used by Mr. Watson-Jones himself, but as he so well points out, the proper understanding of and application of the Thomas splint is still the sheet-anchor in the treatment of fractures of the lower limb.

The writer has no 'bee in his bonnet'. Unlike Bohler who depreciated all open methods of fracture treatment and Lane who saw in open reduction and plating the answer to all fracture problems, Mr. Watson-Jones sets out the arguments for and against open operation and gives clear indications for its use in certain circumstances. Perhaps the only dogma in the book, and it runs right through, is the stress laid on the importance of the patient's active movements for the restoration of function and condemnation of all forms of passive stretching.

Many subjects in bone pathology related to fractures are fully discussed and their relation to particular fracture problems well illustrated. The place of avascular necrosis in relation to fractures of the neck of the femur, the carpal scaphoid and the talus are fully discussed, and the bogey of myositis ossificans is shown in its true light as a subperiosteal ossification of a hematoma and not a muscle ossification at all.

Several subjects outside bone and joint injuries are dealt with. A very full chapter on the vascular traumata associated with fractures such as arterial spasm, Volkmann's contracture and traumatic aneurysm is worthy of study as is the chapter on associated nerve injuries.

If criticism can be levelled against a book so full of well reasoned information, it might be in the section dealing with open and infected fractures. The coloured illustrations in this section are beyond praise, and the principles of wound treatment and drainage by the closed plaster technique are fully discussed, but the actual problem of reducing and maintaining in position badly comminuted war fractures is dismissed in a sentence by saying that 'the displacement of the fractured bone is then corrected by manipulation exactly as if it were a closed injury'. Surely there is a world of difference between manipulating a closed fracture with healthy skin and fractured surfaces which can be got to lock and dealing with a badly comminuted bone, often with bone loss or more than one fracture, surrounded by torn muscle and a large gaping wound. Many of the methods of extension by adhesive strapping or skeletal traction are ruled out by associated injury to the skin surface or the presence of infection. In a future edition, Mr. Watson-Jones might elaborate with the same care as he devotes to simple fractures, just how he sets about dealing with a comminuted lower end of humerus plus fracture of both bones of the forearm. Does he favour attempts at accurate reduction and fixation before the skin surface is healed? What advice does he give to the surgeon in a base hospital seeing a compound fracture from a hospital in the forward area three weeks after the initial wounding when malunion or cross wounding is already in progress? Does he favour breaking down the early granulations in the presence of an unhealed skin wound and attempting to obtain accurate reduction, or does he advocate leaving the fracture alone till healing of soft tissues has taken place, and then correcting the deformity by open operation? It is true that general principles are laid down on this subject in a few scattered sentences, but in a book which deals so fully with all the other difficulties besetting the surgeon who would treat fractures, we would appreciate a little more discussion of this difficult but all too ubiquitous problem.

The last part of the book is given over to the discussion of rehabilitation and the organization of a fracture service. The importance of making rehabilitation purposeful and interesting by team games and competition is stressed, and here more than ever the joyous and vigorous personality of the author comes out in his writings. He radiates encouragement and hope. This is a book to read and re-read. It teaches much more than surgery.

I. M. O.



## BOOKS RECEIVED

1. Sterility and impaired fertility. C. Lane-Roberts, A. Sharman, K. Walker and B. P. Wiesner. Published by Hamish Hamilton Medical Books, London. Price 14s.
2. Orthopaedic surgery. Third edition. W. Mercer. Published by Edward Arnold and Company, London. Price 45s.
3. Non-pulmonary tuberculosis. M. C. Wilkinson. Published by Hamish Hamilton Medical Books, London. Price not stated.
4. Electrocardiograms. Second edition. H. W. Jones and E. N. Chamberlain. Published by John Wright and Sons Limited, Bristol. Price not stated.
5. Demonstrations of physical signs in clinical surgery. Ninth edition. H. Bailey. Published by John Wright and Sons Limited, Bristol. Price 25s.
6. Gas and air analgesia. Second edition. R. J. Minnitt. Published by Baillière, Tindall and Cox, London. Price 5s.
7. A handbook of ophthalmology. Fifth edition. H. Neame and F. A. Williamson-Noble. Published by J. and A. Churchill Limited, London. Price 18s.
8. Medical bacteriology. Fourth edition. L. E. H. Whitby. Published by J. and A. Churchill Limited, London. Price 14s.
9. Industrial nursing. A. B. Dawson-Weisskopf. Published by Edward Arnold and Company, London. Price 5s.
10. Aids to orthopaedic surgery and fractures. Second edition. I. E. Zieve. Published by Baillière, Tindall and Cox, London. Price 6s.
11. Structure and function as seen in the foot. F. W. Jones. Published by Baillière, Tindall and Cox, London. Price 25s.
12. Caesarean section. J. H. Young. Published by H. K. Lewis and Company, Limited, London. Price 16s.
13. Nursing in time of war. Second edition. P. H. Mitchiner and E. E. MacManus. Published by J. and A. Churchill Limited, London. Price 2s.
14. Midwifery for nurses. Third edition. A. W. Bourne. Published by J. and A. Churchill Limited, London. Price 7s. 6d.
15. Brompton hospital reports. Volume XII, 1943. Published by the Research Department of the Hospital. Printed by Gale and Polden Limited, Aldershot. Price 8s. 7d.
16. The Journal of Mental Science, edited by G. W. T. H. Fleming, special number. (Published four times yearly, price 9s.) Published by J. and A. Churchill Limited, London. Price of this special issue is 30s.
17. Ophthalmic surgery and sight testing. M. A. Kamath. Second edition. Published by the author (Planters Lane, Mangalore, S. K. Dt.). Price Rs. 6.

## Correspondence

## INDIAN DEGREES FOR INDIAN GRADUATES

SIR,—I have read with great interest Colonel McRobert's article on the above subject in the *Indian Medical Gazette* of April 1944, pp. 174-177.

It is true that a large number of Indian students go to Europe, especially Great Britain, to obtain higher qualifications for their commercial value in India, particularly because the employers have favoured foreign qualifications.

It is also equally true to say that foreign degrees have higher value in the eyes of the public, and it gives them the impression that the holder has acquired knowledge, skill and sound judgment in his profession.

It is a mistaken notion, and unfortunately quite a large number of people labour under the impression that specialization in general and in the subdivisions of medicine or surgery in particular can be obtained

merely by passing higher examinations or obtaining appropriate diplomas; but this is not the case.

Specialization comes only after long practice and after working under, or watching the work of, specialists in those subjects or subdivisions, such as plastic, neurological, thoracic, endoscopic surgery, etc. I am afraid that in this respect India is very poor, although she has a fine body of general physicians and general surgeons.

People desirous of specializing in such branches of surgery, for some time to come, will have to, or should, visit clinics abroad to obtain the necessary experience and on their return should coach future aspirants to such specialities.

As long as merely passing examinations and obtaining foreign qualifications are considered the criteria of one's knowledge or skill, no progress can be made.

One may ask whether the desire for foreign diplomas should be regulated or unregulated. What other alternative can we offer in the country? Are we to introduce diplomas other than the university degrees? What value should be attributed to such diplomas as compared with university degrees, and by whom should they be granted, and should they be entered in the Medical Register? Should they be given by the Indian Medical Council, in whom is vested the control of medical education in India, by the university or the medical profession?

A young graduate needs sound advice on the subject of post-graduate study and specialization, and this should only be given by people who are qualified to do so by their own long and personal experience. This will save time, energy and money.

Post-graduate education may be defined as any systematic educational activity that help the graduate to keep abreast of the current knowledge and new developments in his own fields.

Nearly all the Indian universities provide advanced training in the medical field and the different universities confer degrees such as M.D. or M.S. upon successful candidates.

The training and regulation of specialists differs in different countries. It is most advanced in the Scandinavian countries, unregulated in France, whilst in Germany the State has left the control of specialization to the medical profession itself. In the United Kingdom the recognition of specialists has been confined almost entirely to the higher qualifications and diplomas of the Royal Colleges and the higher degrees and diplomas of the universities.

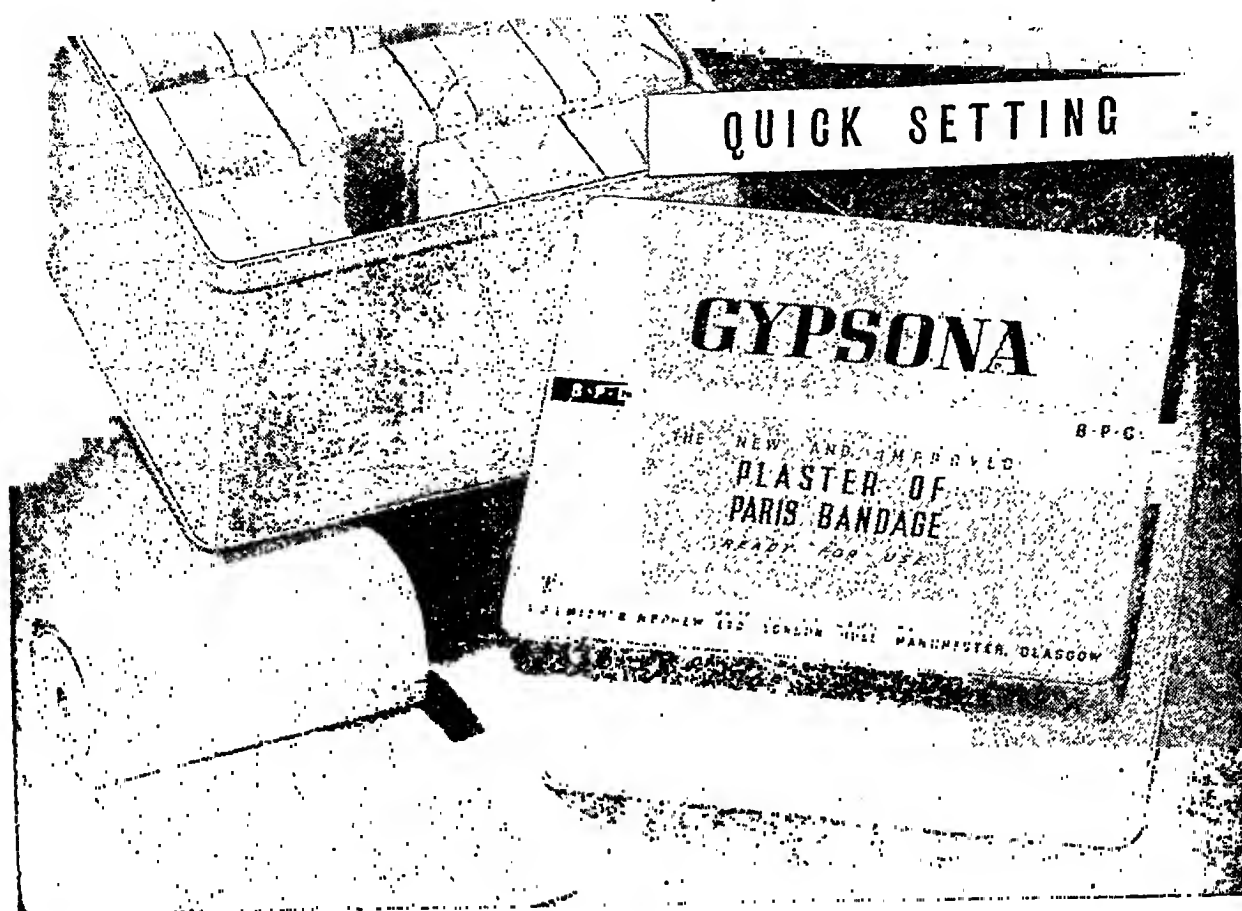
The basic requirements of all the specialities should be:—

- (i) The candidate should be a medical graduate of at least 5 years standing.
- (ii) He should have held a resident hospital appointment for at least one year in an approved hospital.
- (iii) He should have at least two years' training in post-graduate study and practical work.
- (iv) He should pass the higher examination of his university or obtain the recognized higher diploma.

The present system of imparting education needs some overhauling, particularly in the selection of teachers. Professional appointments should not be made on a part-time basis; they should not be given to people engaged in private practice. It is unfair both to the student and the practitioner. The appointments should be full-time ones. The teachers should be well trained and made responsible for the work in their speciality; and they may be allowed selective consulting practice in the hospital only.

Every school or college recognized for post-graduate work should possess well-equipped laboratory, library and museum facilities.

The school or college should be attached to a teaching hospital with a daily average of 200 or more in-patients and an out-patient clinic with an average of 100 or more patients each day. A proportionate reduction will naturally be applicable to institutions teaching one speciality.



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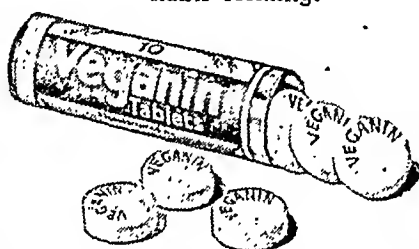
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If the future post-graduate medical education system in India can be modelled on these lines and if the teaching institutions prove worthy of their name and reputation, I am sure the craving for foreign degrees and diplomas will automatically disappear.

I do not wish to leave an impression that I am opposed to medical practitioners going to other countries. They should certainly do so, not with the sole intention of getting a diploma or a degree but rather with the object of enriching their knowledge by the experience of others and establishing contacts with their colleagues abroad.

B. K. SHEOREY, M.B., B.S. (Bom.),  
F.R.C.S. (Eng.)  
LIEUTENANT-COLONEL, I.M.S.,  
Late Surgeon, E. M. S. Metropolitan  
Hospital, London, etc.

NEW DELHI,  
11th May, 1944.

### INDIAN DEGREES FOR INDIAN GRADUATES

SIR,—Lieut.-Colonel G. R. McRobert's special article on 'Indian Degrees for Indian Graduates' is quite welcome for its refreshing thoughts and forcible ideas. He asks 'why then is there such a poor demand for higher degrees from Indian universities? Why is this rush for the M.R.C.P. and F.R.C.S.?' I think the main reason is 'that Governments, Railways and other employers have tended to favour Indian doctors who hold higher European diplomas'. 'Pass diplomas obtained in England such as M.R.C.S., L.R.C.P.', have been preferred for higher posts to 'M.D. or M.S.' of Indian universities. It is not an uncommon experience to find an M.R.C.P. or F.R.C.S. elbowing out a senior M.D. or M.S. in teaching and other hospitals. Even now Insurance Companies prefer one with English 'pass-diploma' to an Indian M.D. or M.S. to examine their proponents over a particular sum. It is not surprising therefore that an average Indian graduate feels that it is more worth while to go to England for a 'higher diploma' than to obtain a higher medical degree of an Indian university with 'the reputation amongst Indian graduates of being so difficult to obtain'.

How then to make Indian degrees more popular to Indian graduates? The chief way is to make Governments, Railways and other employers prefer Indian graduates with higher Indian degrees to those with mere English 'higher diplomas'. Thus M.D. must be preferred to M.R.C.P. and M.S. to F.R.C.S. Unless this change of attitude takes place the 'rush for M.R.C.P. and F.R.C.S.' will continue. I hope the medical authorities of Central and Provincial Governments and Indian universities will note this.

The suggestion that a 'meeting of representatives from the medical staffs of all the Indian universities concerned' is most welcome and is sure to produce far reaching results. Such a conference can remove the reputation of Indian higher degrees 'amongst Indian graduates of being so difficult to obtain', and also to give generous terms to licentiates to obtain university degrees.

S. VENKATESWARA RAO,  
M.D. (Andhra).

AKBARJA BAZARI,  
HYDERABAD-DN.,  
11th June, 1944.

### QUININE SULPHATE FOR INTRAMUSCULAR INJECTIONS

SIR,—May we add two points to our letter on the above subject which appeared in the December 1943 number of the *Gazette*?

1. The new brand of quinine sulphate issued by the Government of Bengal forms a brownish solution when prepared for injections.

We and others have found it perfectly safe and the results are similar to the old brand.

2. We have found that one minim of dilute hydrochloric acid B.P. per grain of quinine sulphate is sufficient to dissolve the quinine. If more is required then either the acid or quinine is at fault.

CHRISTIE MCGUIRE,  
Medical Officer,

M. L. CHAKRAVARTY,  
Assistant Medical Officer,

G. C. KARMAKAR,  
Assistant Medical Officer.

NEWLANDS T. E. AND P. O.  
DOOARS, BENGAL,  
3rd March, 1944.

[Note.—The question of quinine injections was discussed in a recent article in this journal (Lowe, 1944. *Indian Med. Gaz.*, LXXIX, 207). As was said there :—

... if these methods have in view the occasional ease of malaria which needs injection treatment, no objection can be raised, but if it is implied that intramuscular injection is the best method of treating malaria in general, one must protest and protest very strongly.—EDITOR, I. M. G.]

### SULPHONAMIDES AND QUININE

SIR,—Yesterday, while trying to reduce the weight of my baggage by pruning my medical journals, I caught sight of my name in your editorial on Sulphonamides and Quinine.

Somebody has tried to deduct profound discoveries from a passing remark I made in the *Indian Medical Gazette* in 1941 that the two drugs don't agree when given together. My innocent observation was that the patient has his work cut out to keep quinine in his stomach without the added insult of 'M&B'.

In this area we deal with wounded from both war areas, and the occasions on which we are forced to give the two drugs together are many. But if a patient does start vomiting early we just switch over to the mepacrin stage in the standard army course, and he becomes less miserable.

W. NIBLOCK.

92 I.G.H.,  
12 A.B.P.O.,  
4th May, 1944.

## Service Notes

### APPOINTMENTS AND TRANSFERS

LIEUTENANT-COLONEL B. H. SINGH, on reversion from military duty, is appointed as Civil Surgeon, Jalpaiguri.

Captain D. H. Harrison on return from leave resumed charge of his duties as Medical Officer, Khorasan Agency, and ex-officio Vice-Consul, Zahidan, with effect from the forenoon of the 4th May, 1944.

The undermentioned officer is transferred to the General Service Cadre, with effect from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commission)

Captain Har Bhagwan Das. Dated 1st May, 1944.

The undermentioned officers retire with gratuity and are granted emergency commissions from the date specified :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Short Service Commissions)

Captain D. Bhatia. Dated 12th January, 1944.

Captain D. K. Bose. Dated 22nd June, 1944.

The undermentioned I.M.S. officers have been granted emergency commissions:—

INDIAN AIR FORCE—MEDICAL BRANCH

To be (War Substantive) Flight Lieutenants

Madhav Yashwant Alurkar. Dated 23rd September, 1941.

Banoda Kant Bhadury. Dated 21st November, 1941.  
Kshirode Bihari Roy. Dated 28th February, 1942.

6th March, 1942

Maddimsetti Venkataswami Naidu.

Nariman Hormusji Oonvala.

Dossabhoy Bomanji Parakh.

Simadri Prasum Chatterjee. Dated 8th March, 1942.

Mohammed Umar Hayat. Dated 13th March, 1942.

Ranjit Kumar Se. Dated 27th August, 1942.

Hirendra Nath Dutta. Dated 24th November, 1942.

Holavanahalli Anandarao Nagaraja Rao. Dated 20th March, 1943.

Chathapuram Ramayyar Krishnamurthy. Dated 9th April, 1943.

Ambil Tirumala Swamy Srinivasa Iyengar. Dated 14th July, 1943.

Hemendra Nath Sen. Dated 31st July, 1943.

Baldev Singh Khangura. Dated 10th August, 1943.

Laxman Dattatraya Kale. Dated 18th August, 1943.

Bani Kumar Ghose. Dated 23rd September, 1943.

Nani Gopal Sengupta. Dated 14th October, 1943.

Mohammad Masudul Haque. Dated 17th October, 1943.

Gomatam Raghavachari. Dated 17th October, 1943.

Gour Gopal Chatterjee. Dated 4th November, 1943.

INDIAN AIR FORCE—MEDICAL BRANCH

To be (War Substantive) Flying Officers

13th January, 1941

M. M. Shrinagesh. A. Nath.

P. L. Khyrana.

B. Ahmed. Dated 27th February, 1942.

B. K. Mukherjee. Dated 13th October, 1942.

H. S. Gill. Dated 23rd November, 1942.

O. M. Satyendran. Dated 5th December, 1942.

S. K. Das. Dated 8th December, 1942.

K. N. Kothaneth. Dated 12th December, 1942.

W. U. Khan. Dated 8th March, 1943.

A. K. Basu. Dated 15th March, 1943.

R. Jayaram. Dated 16th March, 1943.

G. N. I. Venkatraman. Dated 20th March, 1943.

B. P. Reddy. Dated 15th June, 1943.

22nd July, 1943

M. R. Mahmood. J. H. F. Manekshaw.

G. N. Sen Gupta.

A. M. Shrangpani. Dated 2nd August, 1943.

K. Kurian. Dated 7th August, 1943.

M. Husain. Dated 9th August, 1943.

S. A. Hasnain. Dated 10th August, 1943.

V. B. Tawadey. Dated 12th August, 1943.

H. P. Gnanaolivu. Dated 13th August, 1943.

M. K. Mukherjee. Dated 16th August, 1943.

K. K. U. V. Raja. Dated 20th August, 1943.

M. S. Maini. Dated 23rd August, 1943.

28th September, 1943

B. Bhatia. V. B. Kalra.

D. N. Gupta. H. S. Seth.

D. K. Ray Chaudhuri. Dated 14th November, 1943.

PROMOTIONS

Major to be Lieutenant-Colonel

D. N. Chakravarti, O.B.E. Dated 10th June, 1944.

Captain to be Major

J. R. Vaid. Dated 24th June, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commission)

Captain to be Major

D. Bhatia. Dated 14th March, 1944.

MEDICAL BRANCH

Flying Officers to be (War Substantive)

Flight Lieutenants

M. M. Shringesh. Dated 4th July, 1941.

P. L. Khyrana. Dated 15th August, 1941.

B. Ahmed. Dated 24th July, 1942.

A. K. Basu. Dated 8th May, 1943.

B. K. Mukherjee. Dated 13th May, 1943.

H. S. Gill. Dated 6th July, 1943.

W. U. Khan. Dated 13th July, 1943.

A. M. Shrangpani. Dated 25th September, 1943.

S. K. Das. Dated 5th October, 1943.

G. N. Sen Gupta. Dated 2nd October, 1943.

O. M. Satyendran. Dated 16th November, 1943.

K. N. Kothaneth. Dated 19th November, 1943.

K. K. U. V. Rajah. Dated 2nd December, 1943.

H. P. Gnanaolivu. Dated 28th December, 1943.

B. P. Reddy. Dated 29th December, 1943.

RETIREMENTS

Lieutenant-Colonel Byram Sorabji Dhondy. Dated 2nd June, 1944.

The following retirement with gratuity is permitted and the officer is granted the honorary rank of Lieutenant-Colonel:—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE

(Short Service Commission)

Captain (T/Lieut.-Colonel) P. C. Dhanda. Dated 22nd June, 1944.

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## Original Articles

## CEREBRAL MALARIA

## PATHOGENESIS, SYMPTOMS AND TREATMENT

By R. VISWANATHAN, B.A., M.D., M.R.C.P. (Lond.),  
T.D.D. (Wales)  
LIEUTENANT-COLONEL, I.A.M.C.

*Pathogenesis*

THE most dangerous type of malarial infection is the subtertian or 'malignant' fever. Its clinical manifestations are so numerous and varied as to simulate many other diseases. Among them are what Manson calls the pernicious attacks which the French designate 'accès pernicious'. Of these the cerebral manifestations are attended with the greatest mortality rate; hence their importance.

It is not all cases of subtertian malaria that develop cerebral symptoms; nor do all cases exhibiting cerebral symptoms end fatally. Why is it that only some cases are associated with cerebral manifestations? Why should only some of them succumb and not others? These questions are as puzzling to the physician as similar problems connected with other diseases such as tuberculosis. The question of difference in the strain of the malarial parasite does not arise as the patients on whom I made the following observations were evacuated from the same operational area, many belonging to the same unit. Nor can we bring in the question of constitutional inferiority, as all of them belonged to the same military age-period and were physically fit to carry on the arduous duties of active army life. We have to fall back therefore upon the doubtful explanation of individual susceptibility. It is impossible to say what the actual basis of this individual idiosyncrasy is. Discussion on these lines on such problems which are common to many diseases is, in the present state of our knowledge, fruitless.

The pathological appearances in cerebral malaria that are commonly described in textbooks are: engorgement of blood vessels of the pia mater and brain cortex, punctiform hæmorrhages especially in the corpus callosum, blockage of blood vessels by the sporulating parasites, and focal degenerations or malaria granulomata (Manson-Bahr, 1940). According to Banerjee and Bhattacharya (1943) the blockage of capillaries is also brought about by cloudy swelling and degeneration of the phagocytic cells due to the toxic action of the hemozoin pigment.

Ogurtsova (1940) found, in his three fatal cases, thickening of the walls, desquamation of

the endothelium, impregnation of the walls and blocking of lumen with pigment. He suggests that malarial coma is due to heavy invasion by parasites of the cerebral capillaries, accompanied by a general or local depression of the reticulo-endothelial system. In his opinion the greater vascularization of the cortex provides a wider field for the toxic activity of the parasites, while poor compensation in circulation is the cause of necrosis and hæmorrhage in the white matter. Malkiel (1940), on the findings of seven fatal cases of malaria, concludes that the pathological process in cerebral malaria represents meningo-encephalitis, as he found not only parasites but also exudative and proliferative lesions in the soft membranes and brain tissue. He found granulomata resembling nodular aggregations of glial and mesenchymal elements in other types of infectious encephalitis. In his opinion malarial coma is associated with widespread meningo-encephalitis. While in Ogurtsova's cases the malarial nature of the cerebral disorder was not established clinically, Malkiel's conclusion on the study of his seven cases is 'the course of malarial coma usually manifests a parallelism between the clinical and pathological processes'.

My observations are based on the histopathological appearances of the brain sections in eight fatal cases of cerebral malaria. Of these eight cases, four developed cerebral symptoms during the course of treatment, one after 10 grains of quinine, the second after 40 grains of quinine, the third after 60 grains of quinine and one pill of mepacrine, and the fourth during the plasmoquine stage of treatment. They set up another problem to be solved in the pathogenesis of cerebral malaria. Why should patients develop cerebral symptoms when they are being treated on well-approved orthodox lines? Another question that arises is, why should these eight cases alone out of 44 cases which were all treated with intravenous quinine end fatally? Again it was found that in all these cases parasites disappeared from the peripheral blood within 24 to 36 hours after the institution of treatment. Out of the 8 cases that died, only in one case did we find parasites in the cerebral capillaries. (This case was confirmed by Dr. Bhaskara Menon, Professor of Pathology.) In all others, only pigment was found. The results were confirmed by the Army District Laboratory. Why should these cases die in spite of complete destruction of parasites in the circulation?

Histological appearances of the brain in the present series were essentially the same as those described by other writers except for the following observations. Malarial parasites were not found in the cerebral capillaries except in one case, proved by brain smears and confirmed by sections. Another extremely interesting fact noted was that, in five cases, a well formed ante-mortem clot was found in the sagittal



sinus. As far as I know, sinus thrombosis as a pathological appearance in cerebral malaria has not so far been reported.

The histopathology of the brain seen in my cases did not substantiate the claim of Malkiel's meningo-encephalitis. The cerebral capillaries showed blocking by clumps of red blood corpuscles and malarial pigment. Thickening of the walls and desquamation of endothelium of the capillaries were commonly seen. Punctiform hæmorrhages were seen more in the white matter than in the cortex. They were perivascular in distribution. There was no evidence of inflammation. No areas of necrosis were found. In these cases in which sinus thrombosis was observed, the endothelium of the sinus adherent to the thrombus was found thickened and desquamated. In only one case was the thrombus found filling the whole lumen and thus causing complete obstruction of the sinus and consequent engorgement of the cortical veins. In the other three, only parietal thrombi were seen.

In the untreated cases of cerebral malaria, blocking of capillaries is said to be caused by clumps of parasitized cells. In treated cases, as in the present series, blockage was found in most cases to be due to clumps of cells and pigment without any parasites. To say that the red cells containing the parasites in the various stages of sporulation cannot pass through the capillaries of the brain and therefore cause destruction is not true; for the red cells containing subtertian parasites are smaller in size than normal and even the fully matured parasites are less than the size of a red cell. Localized agglutination of the cells in the capillaries is the cause of blocking. What is the factor that brings about clumping of cells? The finding of sinus thrombosis gives a possible explanation. Clumping of parasites and cells is not the primary factor. It is probably secondary to a tendency to intravascular thrombus formation. The thrombosis in this case is not due to stasis of the circulation, as the blood pressure in most of the cases were normal at the beginning of the cerebral attack. Moreover as Green (1930) points out, stasis of the circulation alone cannot bring about clotting. Evidently it is due to damage to vascular endothelium by the malarial toxin. Pathological appearances confirm this view. There was desquamation of endothelium the cells of which contained pigment; even when there were no parasites, clumping of red cells occurred with entangled pigment in the clot. These facts led us to postulate the theory that endothelial damage by the malarial toxin facilitated intravascular clotting. Complete blockage of the capillaries, especially in the white matter, leads to hæmorrhages which, as has been seen histologically, are perivascular in distribution. The so-called malarial granulomata described by certain writers are nothing but the brain tissue reaction to hæmorrhage and damage to nerve

cells by stoppage of blood supply. They are not pathognomonic, as they bear resemblances to the nodular aggregations of glial and mesenchymal cells seen in other types of infection.

The theory of thrombus formation affords an explanation for death occurring even in those cases wherein complete destruction of parasites occurred, as is evidenced by the absence of parasites post mortem in the peripheral blood in the spleen, and the brain. The presence of pigment in the lumen of the blocked capillaries as well as in the endothelial cells in the absence of parasites suggests that intravascular thrombosis and consequent avascularization of vital centres is the cause of malarial coma and subsequent death. Thrombosis in its turn is the direct result of damage to the endothelium.

In 8 cases out of 44, the cerebral symptoms started during the course of treatment for what appeared to be an ordinary attack of subtertian malaria. In five cases no parasites were found at the time of the cerebral attacks. Three of these ended fatally, and no parasites were found in the cerebral capillaries. And yet blocking of capillaries with R.B.Cs. and pigment was invariably seen, proving the malarial nature of the cerebral attacks. Hence one is inclined to infer that there is some other factor besides the parasites which produces damage to the vascular endothelium and subsequent clumping and blockage. The hypothesis of toxic endothelial damage will explain not only why even fully treated cases of malaria die, but also why some cases during the course of treatment develop cerebral symptoms. That there is a malarial toxin has been postulated on reasonable grounds by malariologists such as Sinton, Manson and others. The nature of the toxin however is unknown.

If intracapillary blockage is the causative factor, how does quinine bring about the disappearance of cerebral symptoms in many of the cases? In the untreated curable cases, the blockage is evidently by parasitized cells, and quinine helps to liquidate them literally and metaphorically, and thus relieve the block. In the treated cases, apparently quinine is powerless, as the block is due to non-parasitized cells and pigment. In all cases however, the clumping of cells is due primarily to damage to the vascular endothelium. The slowing of circulation due to the fall of blood pressure in the later stages of cerebral attacks accentuates the process of thrombosis, and irreparable and irreversible damage is consequently done to the brain tissue.

Briefly stated, the progression of pathological changes will consist in primary damage to the vascular endothelium of the cerebral capillaries, with a consequent tendency to thrombus formation and secondary clumping of cells and pigment. The presence of parasites inside or outside the cells is immaterial so far as clumping is concerned.

### *Incidence*

Two thousand two hundred and fifty-six cases of malaria were treated during the course of 4 months. Out of them, 996 were subtertian malaria cases, 44 of which exhibited cerebral symptoms. Eight developed cerebral attacks during the course of treatment. Eight of the 44 cases ended fatally in spite of vigorous anti-malarial treatment. The incidence of cerebral manifestations comes to be therefore 4.4 per cent with a mortality rate of 16 per cent amongst them.

### *Symptomatology*

The commonest cerebral symptom noticed was coma which was found in 28 cases. A semi-comatose condition was found in 9. Muttering delirium and restlessness were the chief symptoms in two cases. Maniacal attacks were present in three. Two cases exhibited typical signs and symptoms of meningitis, with headache, neck rigidity and positive Kernig's sign. The progression of signs and symptoms is invariably the same in most of the cases with coma. Sudden loss of consciousness while working was the mode of onset in most of the cases. Amongst those who were already under treatment in the hospital, the attack started about an hour after the administration of quinine or mepacrine by mouth.

Coma with epileptiform attacks was observed in two cases. Slight twitchings only, associated with deep unconsciousness, were seen in one case. There was hyperpyrexia in five cases, in all of which there were other cerebral symptoms as well. In the majority of the cases, the pulse was not rapid in the beginning. In only one case was it as slow as 65, though the temperature was 102°F. To start with, the pupillary and corneal reflexes were normal in all the cases except four, all of which proved fatal. Deep reflexes were either brisk or normal except in the above four cases, in which reflexes were sluggish. Plantar reflexes were extensor in nine cases. Blood pressure was normal at the beginning in all the cases except one, in which it was very much raised. In the cases that ended fatally, the pulse became rapid, the blood pressure began to fall, and, as the unconsciousness deepened, pupillary and corneal reflexes were lost and deep reflexes became considerably diminished. Five cases showed epistaxis, and one of them a patch of retinal hæmorrhage as well. The shortest duration of the cerebral attack was 6 hours, while the longest was 48 hours in the non-fatal cases. In the fatal cases, death occurred within a period varying from 24 to 96 hours after the onset of the attack. In only one case did death occur after 10 days.

All non-fatal cases recovered completely after varying periods of convalescence, without exhibiting any of the sequelæ described in textbooks. Some of these sequelæ which have been observed by others are malarial amblyopia,

residual paralysis such as hemiparesis, monoplegia, and psychoneurosis.

### *Treatment*

Intravenous quinine and hypertonic glucose saline was the routine treatment adopted in all the cases. Quinine was repeated in 6 hours in most of the cases. In the majority of the cases that recovered, two injections of quinine proved sufficient to bring about marked amelioration of the cerebral condition, sufficient to enable oral administration to complete the course of treatment. Parasites were found to disappear from the peripheral blood in 90 per cent of cases after two injections. Even in those cases which ended fatally, parasites disappeared after the second injection. In two patients who died, quinine was given intravenously, every four hours. I am of opinion that such large doses of quinine do more harm than good in that repeated injections produce marked depression of the circulation. Lumbar puncture was done as a routine in all those patients in whom the first injection of quinine did not produce any alteration in the general condition. In two cases, even cisternal puncture was resorted to with the hope of relieving pressure. In all the fatal cases, neither relief of intracranial pressure by lumbar puncture nor injections of quinine with glucose saline produced any tendency to check or to slow down the process of progressive deterioration of the patients' condition.

Umanski has advocated intravenous injections of 3 c.cm. of 4 per cent solution of urotropine. He claims that hexamine affects the cerebral functions favourably, though it has no action on the malarial parasite. If it will counteract the effect of malarial toxins on the vascular endothelium, it is worth a trial.

As the pathological findings are mostly the blocking of capillaries in the early stages, any process which will improve the circulation and dilate the capillaries at the same time is bound to be beneficial. Hence Manson's suggestion of inhalation of amyl nitrate at the time of quinine injection coupled with repeated injections of intravenous hypertonic saline and glucose seems to be the rational method of treatment. The addition of sodium bicarbonate will help to combat the acidosis which is invariably present in cases of malarial coma.

### *Reports of fatal cases*

Case 1.—Male Hindu, 22 years, admitted for fever with rigors, duration 5 days. Numerous M.T. rings found in the blood; routine anti-malarial treatment started; on the fourth day of treatment, after he had had 60 grains of quinine and one pill of mepacrine, he became semi-comatose with muscular twitchings. Blood showed very few M.T. rings. Twitchings later developed into typical epileptiform fits. He had four fits that day in spite of intravenous quinine six hourly. In between the fits, twitchings of individual muscles continued. Lumbar puncture done; cerebro-spinal fluid clear, under normal pressure. On the fifth day condition was the same; no M.P. was seen in the blood; three injections of atabrin were given. Sixth day—condition much improved; two injections of quinine

and intravenous glucose saline given; no M.P. seen seventh day; condition very much improved; answers questions; one injection of quinine and 20 grains of quinine by mouth given. Eighth and ninth day, patient conscious; no fits; took medicines and feeds by mouth. Tenth day, patient collapsed with rapid and thready pulse; semi-comatose, no convulsions; no M.P. seen; intravenous quinine and glucose saline given; patient died in the evening.

*Post mortem.*—Spleen slightly enlarged; cut surface deep dark brown; very friable. Liver, intestines, heart, and lungs showed nothing of importance. Brain showed marked engorgement of cortical vessels. A hard greyish brown thrombus, 2½ inches long extending from the vertex to the occipital region, in the sagittal sinus completely occluding the lumen was seen (see figure 1, plate XXI). Cut section showed punctate hæmorrhages in the white matter and the cortex. Microscopically areas of punctate hæmorrhages, and capillaries blocked by clumps of cells and malarial pigment were seen. No parasites found. No parasites in the spleen smear.

*Case 2.*—Male, 23 years; became unconscious with hyperpyrexia of 106 degrees 8 hours after treatment was started for M.T. infection. He had 10 grains of quinine to start with. Growing forms of parasites found in the blood. Four hourly intravenous quinine given. Lumbar puncture done to relieve pressure. No parasites found on the second day. Condition progressively deteriorated. Hypertonic glucose saline given. Deep coma, reflexes sluggish, pupil reflex lost. Cisternal puncture done—slight improvement. Patient died on the third day.

*Post mortem.*—A long ante-mortem clot adherent, found in the sagittal sinus (see figure 2, plate XXI); along the extent of the clot, the meninges peeled off from the brain with difficulty. Cut section showed punctate reddish brown spots in the white matter. Microscopic appearances were: punctate hæmorrhages, capillary blocking, a few parasites seen, endothelium of capillaries thickened and desquamated in places. In some capillaries a distinct thrombus seen adherent to the endothelium.

*Case 3.*—Male, 19 years; brought in unconscious. M.T. infection. Treated with six hourly intravenous quinine; glucose saline and lumbar puncture. Patient died in 43 hours.

*Post mortem.*—Cortical vessels dilated; hæmorrhages seen in the brain; capillary blocking with cells and pigment (see figure 3, plate XXI); no parasites seen.

*Case 4.*—Male, 21 years; M.T. infection; developed coma on the second day after admission; had 40 grains of quinine by mouth before cerebral symptoms started; few parasites only seen at that time. Intravenous quinine six hourly, glucose saline and lumbar puncture. Parasites disappeared in 24 hours. Patient died 48 hours after he lost consciousness.

*Post mortem.*—Meninges adherent to the brain on either side of sagittal sinus—ante-mortem clot found in the sinus; cut section of brain showed hæmorrhages (see figure 4, plate XXI); capillary blocking, endothelial proliferation and desquamation; no parasites; much pigment in the capillaries.

*Case 5.*—Hindu male, 20 years; brought in unconscious; pulse very rapid and feeble; condition grave; very heavy infection with M.T. Blood contained developed forms of parasites. Intravenous quinine six hourly, glucose saline; parasites disappeared in 24 hours; patient died in 36 hours.

*Post mortem.*—Same appearances as in case 4. No clots seen.

*Case 6.*—Male, 21 years; M.T. heavy infection. Lost consciousness after two doses of quinine by mouth. Intravenous quinine six hourly and glucose saline given; parasites disappeared in 24 hours from peripheral blood. Lumbar puncture done on the second day. Patient died on the fourth day.

*Post mortem.*—Meninges adherent along the posterior half of the sagittal sinus. There was a long ante-mortem clot along half of the length of the sagittal sinus (see figure 5, plate XXI). There were two areas

of softening at the points where the meninges were most adherent just adjacent to the sagittal sinus. Punctate hæmorrhages were seen in the white matter and the cortex. Microscopically hæmorrhages, capillary blocking, endothelial thickening and desquamation. Brain and spleen smears showed no parasites.

*Case 7.*—Male, 23 years; brought in unconscious, spleen enlarged, pulse rapid and low volume, pupil reflexes sluggish; blood showed no parasites. Intravenous quinine and glucose saline given; died in 36 hours.

*Post mortem.*—Spleen and brain smears showed malarial pigment, no parasites.

*Case 8.*—Male, 21 years, was treated for M.T. malaria by the routine Army method of treatment. When he was on the plasmoquine course, he developed jaundice; on the last day of plasmoquine treatment he had a rise of temperature, became restless and semi-comatose; blood showed a few M.T. rings. Intravenous quinine given with glucose; condition did not improve; coma deepened. Developed twitchings. Intravenous quinine and glucose given every four hours; patient died on the second day after losing consciousness.

*Post mortem.*—Adherent thrombus at the occipital end of sagittal sinus; punctate hæmorrhages seen in the brain.

### Summary

(1) The pathogenesis of cerebral malaria is discussed on the basis of histological appearances. Primary damage to capillary endothelium by malarial toxin leads to clumping of cells and pigment. The presence of parasites in the cells is immaterial.

(2) The symptomatology as observed in the series of cases is described.

(3) Reports of eight fatal cases are given.

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## DEVELOPING GAMETOCYTES AND SCHIZONTS OF PLASMODIUM FALCIPARUM

### A CASE SHOWING ALL STAGES IN THE PERIPHERAL CIRCULATION

By B. M. DAS GUPTA,

and

S. K. GANGULI

(From the School of Tropical Medicine, Calcutta)

THE gametocytes of *P. falciparum* develop largely, if not entirely, in the internal organs; young forms are rarely found in the peripheral blood. Cases of malignant tertian malaria examined *post mortem* by James (1924) and others showed quite a large number of gametocytes in all stages of development in the bone marrow. Since the introduction of



Fig. 1.—*Case 1.* Cross-section of an organized thrombus in the sagittal sinus. The dark area in the lower and right half of the field is the thrombus (low power magnification).



Fig. 2.—*Case 2.* Sagittal sinus opened out showing a long ante-mortem clot.



Fig. 3.—*Case 3.* Cross-section of a brain capillary blocked by cells and pigment.  $\times 200$ .

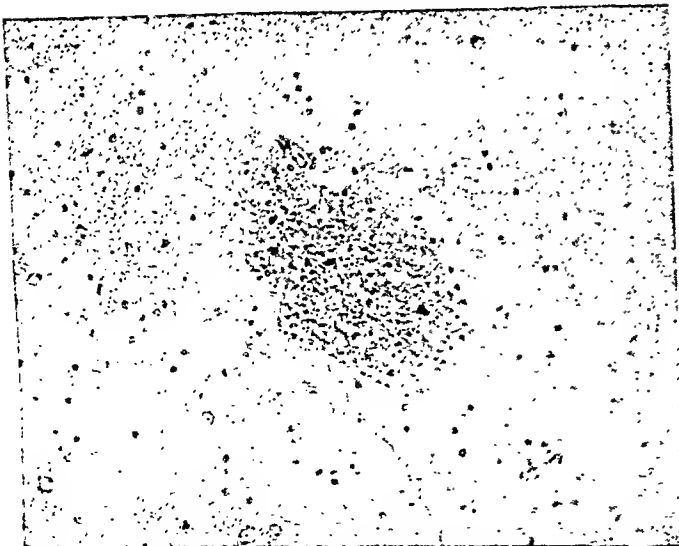
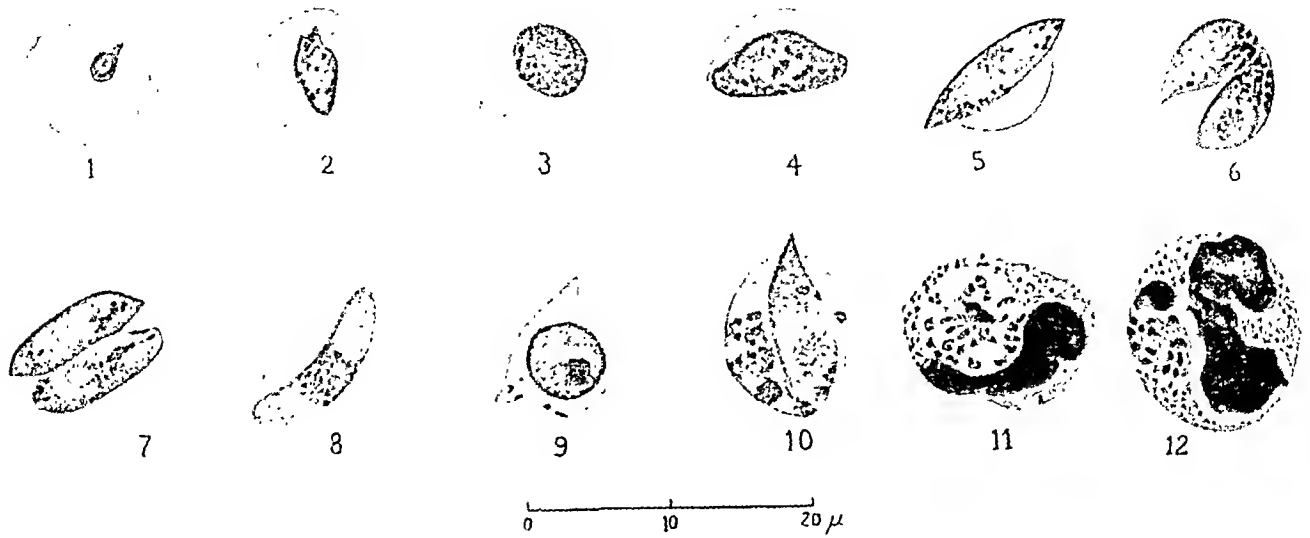


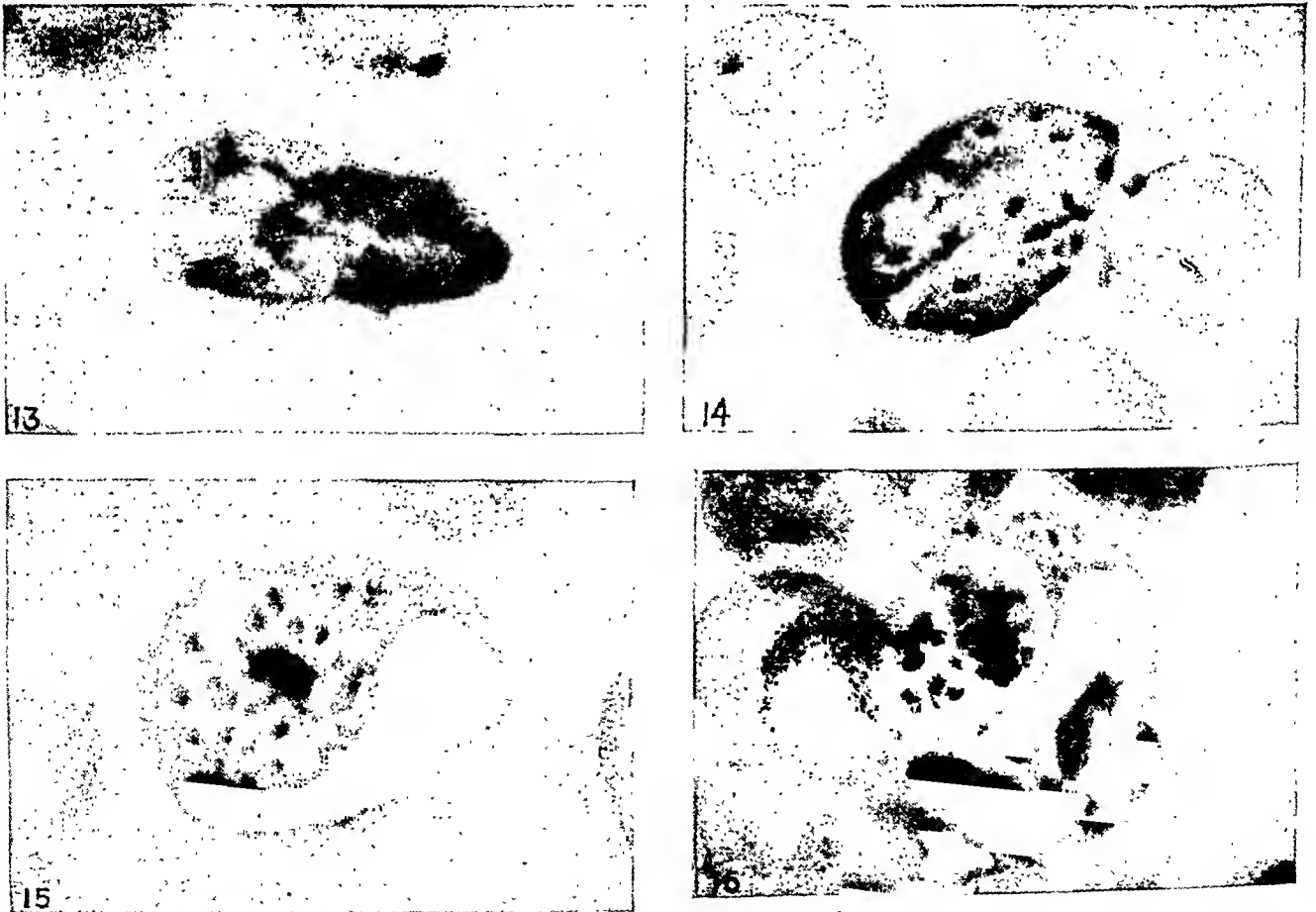
Fig. 4.—*Case 4.* An area of hæmorrhage in the white matter.  $\times 200$ .



Fig. 5.—*Case 6.* Cross-section of a capillary showing endothelial proliferation; a tangential section of another showing a thrombus completely occluding the lumen.  $\times 200$ .



Figs. 1 to 12.



Figs. 13 to 16.



sternum puncture as a method of diagnosis of kala-azar, which is largely used in the school here, it has been found on many occasions that crescents (young and mature forms) were present in the bone marrow smears, although the peripheral blood showed none, or only a few fully developed forms.

These observations indicate that bone marrow is the chief site for the formation of crescents. Developing crescents are also found in the spleen, but in smaller numbers than in the marrow. Recently, while investigating malaria among the famine-stricken population in Calcutta and its environs, a very remarkable case of *P. falciparum* infection came under our observation.

The patient, a young adult, about 25 years old, extremely emaciated, was admitted to one of the hospitals for destitutes shortly before death. Temperature on admission was 99.2°F., the spleen slightly enlarged; the liver not palpable. As the patient was almost unconscious, it was not possible to obtain any information regarding the duration of fever, etc. Blood smears taken 4 hours before death showed a heavy infection with *P. falciparum*—38.6 per cent of the red cells infected. Some of the cells had a multiple infection. Ring forms were predominant. A few schizonts, most of which were phagocytosed, especially by polymorphonuclear leucocytes, were present, but the most striking feature was the occurrence of a large number of developing gametocytes, from very young forms up to those fully mature (see plate XXII). Such a phenomenon, so far as we are aware, was observed only once before and that by Thomson (1912), in a 3-week-old Negro baby. Some of the gametocytes in the blood in the case under report were in pairs in the same corpuscle. This double infection of corpuscles with crescents is of very uncommon occurrence. As mentioned above, the developing gametocytes were much more numerous than the schizonts. The great majority of the schizonts were phagocytosed; the developing crescents, however, some of which were much smaller than the schizonts, were left untouched by the leucocytes.

The question why the leucocytes failed to ingest even the small forms of gametocytes demands an answer. Another interesting point lies in the fact that there is a complete lack of synchronism in the development of the crescents, crescents in all stages of development being found at the same time.

The authors' grateful thanks are due to Dr. C. M. Wenyon, F.R.S., and Colonel H. W. Mulligan, I.M.S., for having examined and expressed their opinion on the specimens of blood smears in connection with this work. They are also indebted to Professor G. Sankaran for the preparation of the photomicrographs used in this paper.

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## THE EARLY DIAGNOSIS OF KALA-AZAR

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### *The importance of kala-azar and its early diagnosis*

KALA-AZAR is a disease which apparently produces periodical epidemics. There were several epidemics during the nineteenth century, and there was an epidemic early in this century which subsided during the period 1920–30, this subsidence being probably accelerated by the effective treatment for the disease which first was introduced during that period. The disease, however, still persists in considerable amount in large areas of eastern India. Moreover, past experience suggests that a fresh outbreak in epidemic form may be seen, and it seems that in many ways the present conditions in eastern India would favour such a recrudescence. Many people who have never been exposed to infection are now being so exposed; recent famine conditions, the widespread malaria, and other factors might possibly help to cause a recrudescence of kala-azar. Reports recently received indicate that such a recrudescence may have already started in some areas.

At present, in the areas where kala-azar is endemic, there are working a large number of doctors, some of whom have had no previous experience of kala-azar. This is particularly so with many medical officers in the army.

The present time therefore seems to be a suitable one for a consideration and a presentation of the methods of diagnosis of kala-azar, particularly in view of the fact that, in recent years, available measures for early diagnosis have very considerably improved.

In the past, diagnosis was usually delayed, often until the 3rd or 4th month of fever, and in fact a certain diagnosis could sometimes only be made after such a period; earlier diagnosis was often impossible, for spleen puncture is advisable only when the spleen is considerably enlarged, and moreover the aldehyde and antimony tests become positive only after this period. In those days, the patients who developed kala-azar frequently suffered from recurring bouts of fever which were either untreated or treated as due to malaria or some other condition for 2 or 3 months, when the general clinical picture and the serological tests which became positive indicated the diagnosis of kala-azar.

This was a highly undesirable state of things which many doctors apparently failed to realize. The opinion was and is still held, and sometimes expressed in medical publications, that kala-azar does not cause death within the first few months, and moreover that the results of treatment of kala-azar are likely to be better and more prompt if the patient has had several bouts of fever before treatment is instituted.

This is a position with which we cannot be satisfied to-day. Recent results of treatment



observed by the writer in very early cases have been excellent, and he is very doubtful regarding the soundness of the view that delay in treatment gives better results and fewer relapses. Moreover, there is no valid reason why any patient should be allowed to suffer weeks or months of debilitating fever when a little more accurate observation by the doctor and the application of methods now available may make the diagnosis possible even within 2 or 3 weeks.

It should not be necessary here to discuss diagnosis of a typical case of kala-azar of three or more months' duration with a history of recurrent bouts of irregular fever, with marked enlargement of the spleen and probably of the liver, with falling out of the hair, pigmentation of the skin particularly the forehead, emaciation, marked anaemia, a rapidly acting heart, granulopenia, oedema of the legs, ascites, bleeding from the gums, possibly jaundice, marked bronchitis, and so on. In such cases in areas where kala-azar is endemic, the diagnosis is very obvious, but, nevertheless, it is surprisingly often missed. We are concerned here with the following problem: how can the diagnosis of kala-azar be made during the first few weeks before the classical picture of kala-azar has developed and possibly before the spleen has become palpably enlarged?

#### Some case records of early kala-azar

Before going on to discuss the problems of diagnosis of early kala-azar, we produce here the summaries of a small series of case records of kala-azar in patients who have recently been seen early in the disease. These case records are not specially selected except that they are early cases of kala-azar.

Case 1.—British military officer, aged 45. Admitted into a military hospital on 27th February, 1944, having been ill for 6 days. There was a previous history of malaria, dysentery and dengue but for the last 9 months there had been no illness of any kind. The patient first noticed that he felt a little cold and shivering and that his legs ached. There were no other symptoms, no headache, no vomiting. For 4 days this went on but he continued his duty. He then developed headache and constipation. On the 5th day he had two shivering attacks and slight abdominal pain but no vomiting. On the 6th day he was admitted into hospital with a temperature of 100°F. which rapidly rose to 103.5°F. with two shivering attacks (see figure 1). The condition on admission was as follows:—

Patient moderately ill, temperature 100°F., pulse 100. No pallor of the mucous membrane, no suffusion of the eyes, throat normal, teeth good, tongue slightly furred; no rash, glands not palpable, chest and heart no abnormality, lungs some basal rhonchi, liver just palpable not tender, spleen neither palpable nor tender. No signs in the central nervous system. Three slides taken showed no malaria parasites. The diagnosis was regarded as possibly typhus or enteric.

During the next 24 hours he had two slight rigors. Examinations of blood for malaria parasites and for bacteraemia revealed nothing. The urine showed no abnormality. The Widal test on this day—To agglutination 1 in 20; the Weil-Felix—negative. Blood examination on this day showed 2,800 white cells, polymorphs 60 per cent, lymphocytes 36 per cent, monocytes 3 per cent and eosinophils 1 per cent.

The subsequent development of the fever is shown in the chart (figure 1). The fever was remittent and irregular, with occasional intermissions and some rigors. Four days after admission the patient's condition deteriorated. He became drowsy and his tongue became furred. Next day he was put on the seriously ill list. His white cell count was then 2,000, red cell 2½ million, the haemoglobin 8.4 gm. He had two rigors early on that day. Albumin was found in the urine. The splenic dullness was found increased but the spleen was not palpable. There was some pain in the abdomen.

A review of the case on this day, 4 days after admission and the 11th day of the illness, suggested four possibilities—malaria, typhoid, kala-azar and acute miliary tuberculosis, but either typhoid or kala-azar was considered to be most likely. The negative blood culture and agglutinations and the irregular nature of the fever were against typhoid, but the illness appeared to be very acute and the patient too ill and toxic for kala-azar. On the same day the patient passed stools which were described as typical pea-soup stools. Further blood cultures taken on this day were negative; the aldehyde and antimony tests were negative; stool culture was negative and urine culture showed *B. coli*. The white cells now numbered 3,400 with 60.5 per cent polymorphs. To agglutination had now risen to 1 in 80.

Two days later sternum puncture was done, and examination for *L. donovani* in the material was carried out in three different laboratories. Only one laboratory reported very scanty *L. donovani* present, but the report was not received for 4 days due to postal delays. During these days the patient remained seriously ill; he was restless and drowsy; he developed hiccup and twitchings and showed râles at the base of the lungs; some rigors occurred. To agglutination rose to 160.

On the 19th day of the illness sternum puncture was repeated and once more *L. donovani* were found in very small numbers. On the same day the complement-fixation test for kala-azar was performed and was positive 1 in 25. The aldehyde and antimony tests were both negative. The spleen was still not palpable.

Antimony injections were started for kala-azar. Within 24 hours the temperature fell below 100°F. and

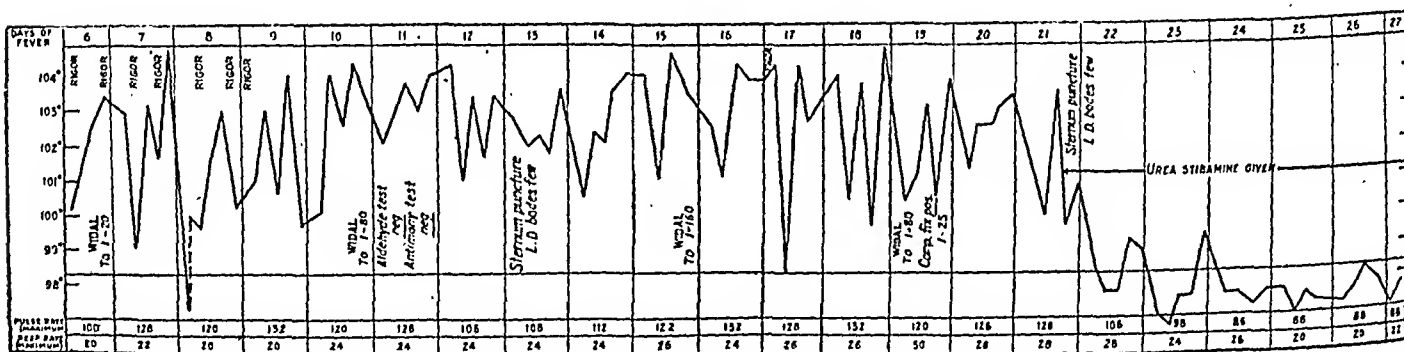


Fig. 1.—Case 1.

by the 3rd day of treatment the temperature touched normal and remained practically normal from then onwards. The response to treatment was dramatic. Four weeks later at the end of the course of urea stibamine the patient's general condition was practically normal but there was considerable anaemia. Red cells were  $3\frac{1}{2}$  million and haemoglobin 8.8 gm.

The noticeable features of this case are: (a) the acute onset with rigors and considerable toxæmia, (b) the irregular nature of the fever, (c) the absence of palpable enlargement of the spleen, (d) negative aldehyde and antimony tests, and (e) the rise in To agglutinins but not to diagnostic level. The diagnosis of kala-azar was indicated only by the nature of the fever and the presence of leucopenia, and was confirmed by finding the *L. donovani* bodies in sternum puncture and by the complement-fixation test.

Case 2.—An Anglo-Indian male, aged 16, admitted into hospital on 28th September, 1943, with a history of fever for 10 days, loose motions with blood and mucus in the stool for 10 days, and pain in the epigastrium for 4 days.

The previous history showed nothing of any consequence. The temperature on admission was  $99^{\circ}\text{F}$ . and rapidly rose to  $102^{\circ}\text{F}$ . and for the next 8 days he had an irregular remittent fever which suddenly subsided and returned to normal. The liver and spleen were both enlarged and palpable on admission and later. There was pain and tenderness in the epigastrium and also tenderness in the sigmoid; *E. histolytica* were demonstrated in the stools. There was no granulopenia; the white cell count was 6,875 with 62 per cent polymorphs and the red cell count was 5 million with haemoglobin 88 per cent (Hellige). The aldehyde, antimony, and complement-fixation tests for kala-azar were all negative. There was no obvious cause for the fever but the patient had *E. histolytica* infection and was treated for this and was later discharged from the hospital.

Later, he returned with a fever similar to the previous one which had returned after an afebrile period lasting about 8 weeks. His liver and spleen were found enlarged; no other findings of importance were made. The general condition of the patient was good. The temperature, pulse rate, etc., are shown in the chart. The red cell count was 4 million, haemoglobin 88 per cent and the white cell count was 9,000. Aldehyde, antimony and complement-fixation tests for kala-azar gave negative results, but sternum puncture revealed *L. donovani*.

Treatment for kala-azar was immediately instituted. The temperature fell to normal in 3 days, and recovery was uneventful, all the symptoms being controlled, the spleen and liver enlargement disappearing.

The striking features of this case are as follows: the absence of any leucopenia during both the first and second febrile attacks caused by kala-azar and also the absence of any appreciable degree of anaemia. The negative results with the usual kala-azar tests even including the complement-fixation test and even 3 months after the original onset of the fever. The clinical picture was that of kala-azar, particularly the nature of the temperature and the spleen and liver enlargement, and this was entirely unsupported by any laboratory finding until the sternum puncture was done.

Case 3.—The patient, a Hindu male, aged 17, came to our out-patient department with a history of vague fever with chill for about 3 weeks. There was no previous history of any consequence. There was some enlargement of the spleen, some pigmentation of the face and some bronchitis. The patient was suspected to be suffering from kala-azar and was recommended for hospital admission, but owing to the lack of accommodation the patient was not admitted for 2 weeks, i.e. 5 weeks after the original onset of the fever. By that time the fever had subsided. The patient's general condition was good. The spleen was slightly enlarged; the liver was not palpable; there was some cough, and some rhonchi in the chest and slight bleeding from the gums. The white cell count was 5,900, neutrophils being 70 per cent and the red cell count  $3\frac{1}{2}$  million, haemoglobin 40 per cent (Hellige). The aldehyde and antimony tests gave negative results, and the only laboratory finding indicating kala-azar was a positive complement-fixation test. Sternum puncture was done and *L. donovani* in fair numbers were demonstrated; treatment was instituted and recovery was uninterrupted.

The lack of granulopenia, the negative aldehyde and antimony tests were striking features of this case.

Case 4.—Anglo-Indian female, aged 10, came with a history of fever of 7 days' duration. The previous history contained nothing significant. The spleen and liver were just palpable, and there were no other clinical findings of importance. The patient was admitted into hospital with a temperature of  $103^{\circ}\text{F}$ . and the subsequent development of the fever, with the pulse and respiration rates, is indicated in the chart (see figure 2). From the beginning the case was regarded as possibly typhoid but the Widal test on the 8th day was negative; repeated on the 13th and 18th days of the fever it was also negative. On the 10th day of the fever the white cell count was 4,800 with 60 per cent polymorphs, and haemoglobin was 10.3 gm.

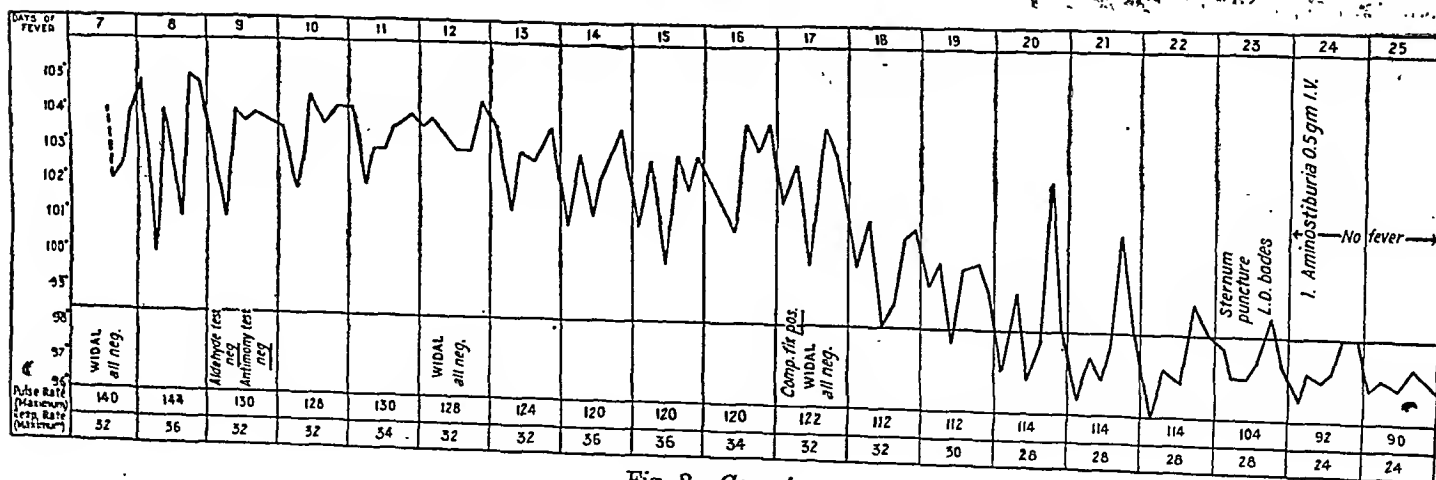


Fig. 2.—Case 4.

On the 9th day of the fever the aldehyde and antimony tests were negative; blood cultures were sterile. Thus there was no indication of kala-azar except the nature of the temperature chart. On the 17th day of illness the complement-fixation test for kala-azar was done and the result was positive. Four days later sternum puncture was done and *L. donovani* were found. Treatment was instituted and recovery was uninterrupted.

The striking facts about this case were that while the temperature chart suggested kala-azar there was no definite granulopenia and the serological tests were negative; except that the complement-fixation test done on the 18th day was positive and this finding was confirmed by the finding of *L. donovani* in sternum puncture.

Case 5.—A Hindu female, aged 30, came with a rather vague history of fever for 4 months. The liver was palpable and the spleen was felt 3 inches below the costal margin. The clinical appearance suggested kala-azar and the patient was admitted into hospital. The temperature, pulse and respiration rate are shown in the chart (see figure 3). As seen, the fever was irregular and the pulse rate was persistently high. A few days after admission to hospital the patient's respiration rate increased markedly and there was definite evidence of bronchio-pneumonia. The patient became very ill. Treatment with M&B 693, the administration of oxygen, etc., was followed by some clinical improvement, but the respiration rate remained high and it cannot be said that the response to M&B 603 was striking, moreover the fever persisted. Finally the temperature subsided after about 2 weeks in hospital to about normal. During this time the white cell count varied between 3,000 and 4,000 but the polymorphs were only 35 per cent. The red cells on different occasions numbered from 2.8 to 3.5 millions and the haemoglobin was about 60 per cent. The aldehyde and antimony tests were negative. Complement-fixation test gave a doubtful result. Blood and urine cultures were sterile and Widal was negative. All other findings were negative. After a period of convalescence the patient was discharged from the hospital with no definite diagnosis but 'early kala-azar' was written on the chart. It was later learnt that the patient had a return of the fever, that the aldehyde test was positive and that treatment with antimony produced prompt recovery.

The striking features of this case are as follows: The clinical findings suggested kala-

azar—the nature of the temperature chart, the enlargement of the spleen and liver and granulopenia, but all laboratory tests for kala-azar gave negative results including sternum puncture except that the complement-fixation test was doubtful.

#### Conclusions from these records

We will first outline the general conclusions and then consider details.

#### A. General

In the diagnosis of kala-azar in the early stages, i.e. during the first or possibly the second febrile attack, the following findings are the most important.

(i) *The nature of the fever.*—The irregular temperature, the relatively rapid pulse rate, the absence of marked toxæmia, etc. This has been characteristic in all the cases seen.

(ii) *The finding of *L. donovani* in sternum puncture.*—This is usually possible in genuine cases of kala-azar, but it should be noted that in one of the cases reported here no *L. donovani* were found and in another case there were so few that half an hour's search was necessary before one was found, and hours of search revealed only three.

(iii) *The positive complement-fixation test.*—This also is not invariably found in the cases recorded here. One was negative and one was doubtful in the early phase of the fever although later in the fever practically all cases give positive results.

These three findings are the most constant and the most valuable in the early diagnosis of kala-azar. One would hesitate to diagnose kala-azar in the absence of all the three, or in the absence of the second if either the first or the third was also absent.

The following signs if present are of some diagnostic value but if absent do not rule out early kala-azar:

(iv) Splenic enlargement.

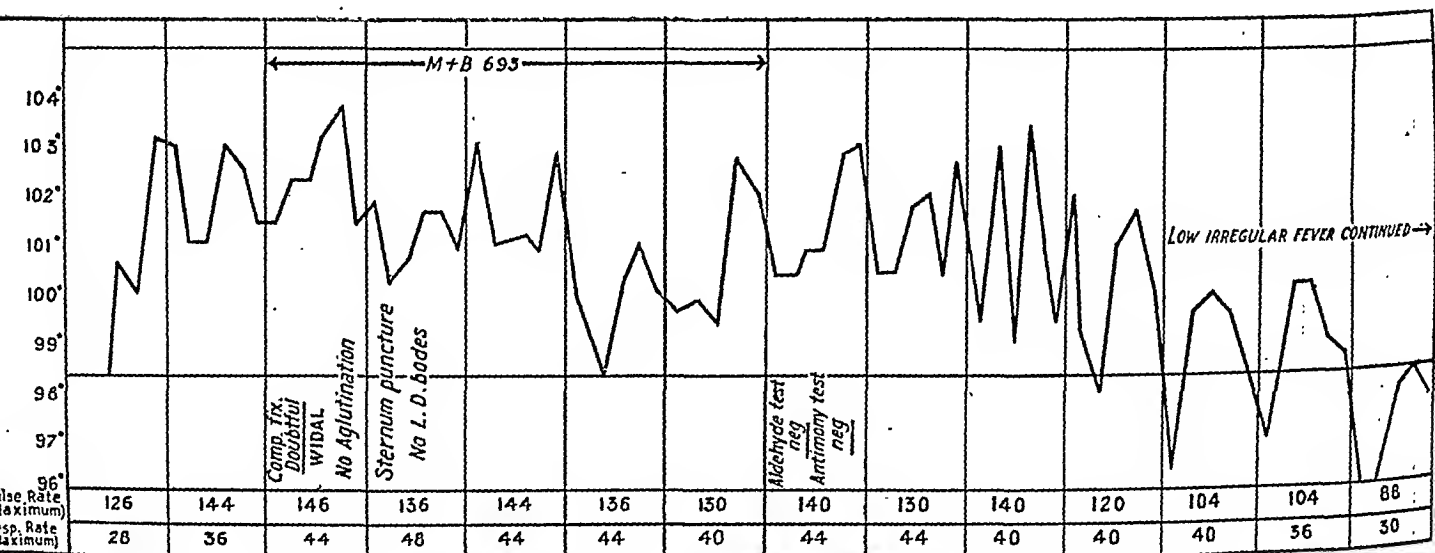


Fig. 3.—Case 5. (Not diagnosed till later.)

- (v) Liver enlargement.
- (vi) Leucopenia.
- (vii) Positive aldehyde test.
- (viii) Positive antimony test.

Any or even all these may be absent in the early stages of kala-azar.

### B. Special points

*The nature of the fever.*—This on the whole is the most valuable indication of the presence of kala-azar with the exception of the actual demonstration of *L. donovani*. Accurate records of temperature, pulse and respiration rates, recorded if possible 4-hourly, are of the very greatest use. The following are the main points to be observed.

The fever of kala-azar is extremely variable; variable in its onset, variable in its development and in its termination. In fact, the characteristic of the fever of many cases of kala-azar is its irregularity. It has characteristically none of the regularity of the typhoid fever chart; the more periodic irregularity of the malaria chart is lacking. In fact, the suspicion of kala-azar is often aroused because the temperature chart does not look like that of any of the better known diseases. Nevertheless the textbooks describe the onset of the fever of kala-azar as being of three main types—the insidious type, the enteric like and the malaria like.

Regarding the latter two types it can usually be said that the resemblance of the temperature chart to that of enteric or malaria is often not very close, and that there are usually certain features in the chart which are rare in either of these two diseases.

In the 'insidious' type, the onset of the disease is difficult to describe because it is rarely seen in hospital. The patients describe mild attacks of irregular fever which does not seriously incapacitate them although they feel unwell.

The 'typhoid-like' onset is characterized by a steady rise of temperature for several days, but even here during the period of onset there are often chills and even definite rigors and also remissions which are not seen nearly so commonly in typhoid; when the fever reaches its height, rigors and remissions may become very frequent, the temperature rising and falling 2 or 3 degrees sometimes twice a day or even three times a day, so that the resemblance to typhoid is often not at all close.

In the 'malaria-like' onset, the onset may be sudden with a feeling of chill and definite rigors and a rapid rise of temperature, but within a day or two the differences between the fever and that of malaria will be clearly seen. There is no regular periodicity about the chart. Moreover the absence of other symptoms to be discussed later will usually weigh heavily against malaria.

In areas where malaria is endemic, malaria parasites may sometimes be found in the blood of such a case of kala-azar, but they are not

sufficiently numerous to cause the fever, and moreover the fever persists after the administration of quinine.

The duration of the bouts of fever caused by kala-azar is very variable but is usually between 2 to 4 weeks. The fever usually falls gradually but it may disappear quite suddenly almost with crisis as in case 2.

In between the definite bouts of fever, the temperature may be normal or even sub-normal, and the duration of the apyrexial period may be very considerable, several weeks or even longer. In the two such cases reported here it was about 2 months. The original attack of fever may be wrongly attributed to typhoid, and the recurrence of fever may be attributed to relapse of typhoid as was seen in one case recently. In the later febrile attacks, remissions and intermissions are said to be seen even more commonly than in the original febrile attack, and the classical double rise of temperature in 24 hours is said to be more common in the later attacks. In our experience these features are often detectable even in the first attack.

*Other symptoms accompanying the fever.*—In the initial febrile attack caused by kala-azar and also in the second or even the third febrile attack, other symptoms may not be marked, are very slight, or are completely absent. Perhaps the commonest symptom is a certain amount of bronchitis. There is often a complete absence of the severe headache, the pains in the back and in the limbs which are characteristic of malaria. There is as a rule very little of the toxæmia which is characteristic of typhoid. Mentally, the patient is usually bright, the appetite is relatively good, the tongue relatively clear and the gastro-intestinal functions normal. In fact, many patients even with a temperature of 102°F. or higher may feel fairly well and attempt to carry on work, as in case 1 reported here. This absence of symptoms accompanying the early fever is characteristic of kala-azar. A patient with high fever will feel weak and his pulse will usually be rapid but there is often nothing else of note. Occasionally however in early kala-azar considerable toxæmia, may be seen, as in case 1, and of course late in kala-azar, toxæmia and complications may be serious.

*The finding of *L. donovani* in sternum puncture.*—This is the most accurate of all methods of early diagnosis of kala-azar, although occasionally the parasites may be so few as to escape detection. In a patient such as in case 5 reported here in which the clinical findings strongly indicated kala-azar, the diagnosis would probably have been justified in the first attack although *L. donovani* were not found in the sternum puncture. Such cases however are rare.

The finding of *L. donovani* in sternum puncture material is a matter demanding a little care and experience. The technique of sternum puncture need not be detailed here. The commonest mistake is to draw too much blood into the syringe. It is best to

stop suction as soon as blood begins to appear at the proximal end of the needle. Further suction will only introduce blood into the material, will dilute the sternal material and will make the detection of *L. donovani* more difficult.

The smear is made in a manner very similar to that used for the thin blood film for malaria. The film may be stained with Leishman, Giemsa stain, or a combination of the two, but the author has found that a very much more rapid and equally satisfactory method is to fix the film with a few spots of methyl alcohol and stain with the rapid method of Field (1941). The parasites are found most readily in the leucocyte edge and in the 'tails' of the film. Very prolonged search may be necessary in several films before *L. donovani* are found, but in some cases even early in the disease they are found in considerable number with little difficulty.

*The positive complement-fixation test.*—The nature of this test and its application in kala-azar need not be discussed here. It is hoped that the present author is not prejudiced in favour of this test by the fact that he was the first to apply it in kala-azar in India, having read of the positive results obtained in South American kala-azar. A thorough working out of the application of this test in kala-azar has been done by Sen Gupta, whose writings on the subject should be studied\*. The findings are that it is a test of high specificity, giving positive results in kala-azar far more constantly and also much earlier in the disease than the aldehyde or antimony tests. In a very few cases, however, of definite kala-azar, the test has given doubtful or negative results.

At present the soluble antigen is not available on the market, but the kala-azar department of the School of Tropical Medicine would be very pleased to do the complement-fixation test in cases of early kala-azar if the serum is sent sterile in ampoules and if complete clinical details of the case are sent with it.

It is often useful to consider the sternum puncture findings and the results of the complement fixation together. A positive or doubtful complement-fixation test may make one search sternum puncture films for one hour or more, instead of the usual half an hour, and may thus lead to the detection of *L. donovani* in cases in which they would otherwise be missed.

*Splenic enlargement.*—Unless the spleen is previously enlarged as the result of chronic malaria, the spleen does not normally become palpable during the first few weeks of the onset of kala-azar. Thus the palpation of an enlarged spleen cannot be relied upon early in the disease, and the absence of such enlargement does not rule out kala-azar if the fever is of a relatively short duration. If, however, the fever is of long duration, 2 or 3 months, or if two or three febrile attacks have occurred with an interval between them, the absence of palpable splenic enlargement will be evidence against the diagnosis of kala-azar. In case 1 reported here the spleen never became palpable but the splenic dullness

increased. Such increase, however, may be seen in many fevers. The characteristics of the enlarged spleen of kala-azar have frequently been described and need not be discussed here.

*Liver enlargement.*—In the really early phase of kala-azar, liver enlargement may be detectable, perhaps even more commonly than splenic enlargement, probably because the slight enlargement of the liver makes it palpable whereas considerable enlargement of the spleen is necessary to make it palpable. The slight enlargement of the liver is, however, seen in several febrile diseases and its value in diagnosis is very limited.

*Granulopenia.*—As the cases here recorded show, granulopenia may be completely absent in the first few weeks of kala-azar. In case 2 quoted here it was probably the absence of granulopenia, and in fact the presence of slight leucocytosis, which prevented the diagnosis of kala-azar being made in the first febrile attack. This is a fact which is not usually mentioned in the descriptions of the disease and one which deserves to be more widely known. While discussing this subject it may be mentioned that the word 'granulopenia' is much more informative and accurate than the term 'leucopenia with relative lymphocytosis' which is often used. The absence of the eosinophils which is described as characteristic of kala-azar is frequently not found early in the disease.

The changes in the white cell count cannot be relied upon for early diagnosis of kala-azar. Their presence is of value; their absence does not rule out kala-azar.

*The red cells.*—In the early cases of kala-azar seen here, anaemia has been a much more constant finding than the granulopenia but nevertheless counts of 5 millions and over have been made. In most cases some degree of anaemia has been seen, and it tends to be macrocytic and hyperchromic, but there are so many other possible causes of anaemia in our patients, that the blood picture is of little value in diagnosis.

*The aldehyde test.*—In early kala-azar, the test is of very limited value. If we wait for a positive aldehyde test for the diagnosis of kala-azar, most cases will not be diagnosed for three months or more, and some cases will not be diagnosed at all, for even in advanced kala-azar the aldehyde test may be negative. In one patient recently admitted into this hospital, nearly moribund with kala-azar of 6 months' duration, the aldehyde and antimony tests gave doubtful results. Moreover, a positive aldehyde test may be seen in other diseases, and the test, though a valuable one, has quite serious limitations. It can be said, however, that a patient with marked enlargement of the spleen and a negative aldehyde test is probably not suffering from kala-azar.

*The antimony test.*—The remarks already made about the aldehyde test apply equally to the antimony test.

\* His findings up to date are recorded in this issue.—  
Editor.



*Summary and conclusions*

1. The importance of early diagnosis of kala-azar is emphasized.

2. Case notes are given of several typical early cases of kala-azar seen in Calcutta, and the findings made in these cases are discussed.

3. The most constant finding in these cases has been the irregular temperature of remittent nature with a relatively rapid pulse rate and the absence of marked toxæmia.

4. The only other findings made with a high degree of constancy in early cases are the finding of *L. donovani* in sternum puncture and the finding of a positive complement-fixation test. Even these findings are occasionally not made.

5. The other findings frequently regarded as characteristic of kala-azar—splenic enlargement, liver enlargement, granulopenia, positive aldehyde test or antimony test—are frequently not found early in the disease. The absence of any or all of these in a fever of a month's duration or less should not rule out the diagnosis of kala-azar, and even later some of these signs are often absent.

6. In the early diagnosis of kala-azar the general clinical picture and the nature of the fever are the most important considerations; sternum puncture with staining for *L. donovani* provides the most reliable method of confirmation. The complement-fixation test done with the WKK antigen or some modification of it is the next most useful confirmatory measure. With sound clinical observations and the use of these tests, diagnosis should usually be possible within 3 weeks of onset.

My thanks are due to Dr. P. C. Sen Gupta for doing the complement-fixation tests and sternum puncture examinations; to Dr. R. N. Chaudhuri, and to the officer commanding a military hospital for information quoted here.

## THE VALUE OF THE COMPLEMENT-FIXATION TEST IN THE DIAGNOSIS OF KALA-AZAR

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In a previous publication (Sen Gupta, 1943), the results of the complement-fixation test using the original Witebsky, Klingenstein, Kuhn (WKK) antigen were reported. Reference was also made about the preparation of the antigen according to the WKK method. It was shown that a complement-fixation test of marked degree of 'specificity' for kala-azar had been evolved. In order to investigate further the value of the complement-fixation test in the diagnosis of kala-azar, it was decided during last year to include this test in the routine investigation of all cases referred to the kala-azar out-patients clinic or the kala-azar research department of the Calcutta School of Tropical Medicine.

The antigen used in this investigation was not, like the original WKK antigen, prepared from the human tubercle bacillus. The work of Dharmendra and Bose (1941) had shown that with antigens prepared from various acid-fast bacilli, viz *Mycobacterium phlei* and the so-called leprosy bacilli of Kedrowsky, Lleras, Bayon and Duval, complement-fixation reaction similar to that with the original WKK antigen could be obtained in leprosy and in leishmaniasis. Due to some practical difficulties in obtaining adequate quantities of growth of the human tubercle bacillus, it was decided to use an antigen prepared according to the WKK method from Kedrowsky's bacillus. Kedrowsky's bacillus was chosen because there is a luxurious growth of this bacillus on glycerine broth within 3 weeks. Through the courtesy of Dr. Dharmendra several batches of this antigen were prepared for us by Mr. R. Bose the chemist of his department.

The technique adopted was essentially the same as used in the case of the WKK antigen.

The complement-fixation test using the antigen prepared from Kedrowsky's bacillus has been carried out for about 9 months now, and the total number of patients investigated is over 900. The majority of the cases was from the kala-azar out-patient clinic of the school. Other sources were the wards of the hospital of the school, the different military hospitals, and Jadabpur Tuberculosis Hospital. The syphilitic sera (Kahn test positive) were obtained from the Red Cross Blood Bank, Calcutta, and the sera of filariasis patients from the filariasis clinic of the school. Group (a) of the control cases consisted of acute and chronic malaria, splenic anæmia, 'Bengal splenomegaly', myeloid leukæmia, enteric fever, and various other febrile and afebrile conditions.

The analysis of the results of the complement-fixation test is given in table I. It will be seen that the test was positive in 93 per cent of all cases of kala-azar; 6 per cent of kala-azar cases gave a doubtful reaction and in 1 per cent the test was negative.

Of the control cases, group (a) contains, among others, sera from patients suffering from the different diseases that are generally considered in the differential diagnosis of kala-azar. In this group, 99 per cent of cases gave a negative reaction and in 1 per cent (6 cases) only a doubtful reaction was obtained. These 6 cases could not be followed up, but from their history at least 3 of them might well have been cases of kala-azar, and 2 of them were cases of cirrhosis of liver.

The filariasis group (c) and the syphilis group (b) did not give rise to a single positive or even a doubtful reaction. Of 20 cases of chronic pulmonary tuberculosis from the Jadabpur Tuberculosis Hospital group only 2 cases gave a positive reaction.

The whole control group does not contain any sera from leprosy cases.



*Specificity of the reaction.*—From the above analysis it will be seen that the result is negative in at least 99 per cent of all cases likely to be considered in the differential diagnosis of kala-azar and positive in 93 per cent of all cases of kala-azar.\* If we regard a doubtful reaction as an indication for further investigation, clinical and parasitological, for kala-azar, we are likely to be able to spot 99 out of a 100 cases of kala-azar with the help of this test. The fact that a positive reaction is occasionally obtained in obvious cases of chronic pulmonary tuberculosis should not be regarded as a serious

disadvantage in common, that they do not give a positive reaction before the disease has run for several months, 2 to 6 months in most instances. During the period of pyrexia simulating enteric fever or malarial fever at the onset of kala-azar, none of these tests is of the slightest help. The clinical features, negative findings for enteric fevers and malaria among others, arouse the suspicion of kala-azar at this stage. Except for sternal puncture which is positive in a maximum of 89 per cent cases, there is no means of confirming the diagnosis. From table I it will be seen that in no less than

TABLE I

*Analysis of results of complement-fixation test for kala-azar, using an antigen prepared according to Witebsky, Klingenstein and Kuhn method from Kedrowsky's bacillus*

		COMPLEMENT-FIXATION TEST		
		Positive	Doubtful	Negative
I. <i>Kala-azar</i> cases—				
Aldehyde test 'positive' ..	161	150	10	1
Aldehyde test 'doubtful'; diagnosed by finding leishmania (32 cases) and on clinical grounds (25 cases).	57	53	3	1
Aldehyde test 'negative'; diagnosed by finding leishmania (29 cases) and on clinical grounds (13 cases).	42	38	3	1
TOTAL ..		260	240 92.6% (93%)	16 6.1% (6%) 3 1.1% (1%)
II. <i>Control</i> cases—				
(a) Miscellaneous diseases (febrile or afebrile with or without enlargement of liver and spleen).	604	..	6	598
(b) Kahn test positive sera ..	16	..	..	16
(c) Filariasis cases ..	20	..	..	20
(d) Chronic pulmonary tuberculosis ..	20	2	2	16
TOTAL ..		920 cases		

handicap. Such cases should be excluded by the history, clinical features and also skiagraphy and bacteriological examination if necessary.

After all, the chances of a false positive or doubtful reaction with this test is much less than with the Wassermann reaction (WR) where a false positive reaction is obtained in quite a large number of conditions (Greval, Sen Gupta and Das, 1938).

*The value of the test in the early diagnosis of kala-azar.*—The well-known serum tests, viz the aldehyde test, the antimony test and the globulin precipitation test, have the one great

38 out of 42 cases, a positive reaction was obtained in the group of cases showing completely negative reaction with the aldehyde test, and the reaction was doubtful in 3 and negative in one case only.

Table II shows the duration of illness as given by the patients, the size of the spleen, liver and the mode of onset, etc., of this group of cases. It will be seen that in 4 cases a positive reaction was obtained within 3 weeks, and in 5 more cases within one month to 6 weeks. In 14 cases a positive reaction was seen in patients with slight or no splenic enlargement (varying from 'not palpable' to 1½ inches below the tip of the 9th left costal cartilage) without any marked degree of hepatic enlargement. In these cases the disease was undoubtedly in an early stage.

If we consider the 'aldehyde doubtful' cases (see table III) it will be seen that in at least 6 of the patients who could give an idea as to the

\* It will be seen that with this antigen the percentage (93 per cent) of all kala-azar cases yielding a positive reaction is distinctly less than that obtained with the original WKK antigen (97 per cent) (Sen Gupta, *loc. cit.*). This induces us to hope that with the antigen prepared locally from human tubercle bacillus, even better results may be obtained.

onset of illness, the duration was  $1\frac{1}{2}$  months or less. In 24 cases the spleen was 2 inches or less below the tip of the 9th left costal cartilage. These cases were also fairly early cases and the complement-fixation test was positive in 23 instances and doubtful in one case only.

From the above discussion, it will be evident that in over 90 per cent of very early cases of kala-azar, a positive reaction was obtained with this test. Barring spleen puncture where there is about 95 per cent chance of finding the parasite but which procedure is usually impossible in the early stages of the disease since the spleen is not sufficiently enlarged, no other method of diagnosis gives a positive indication of kala-azar in so high a percentage of cases. Even with the best possible technique and most painstaking search, the proportion of positives in sternal

TABLE II  
'Aldehyde-negative' cases of kala-azar

Serial number	C. F. test	Spleen, inches	Liver, inches	Duration of illness	Type of onset
1	++	$1\frac{1}{2}$	$1\frac{1}{2}$	4 months	Malarial, cancrum oris +.
2	++	5	3	3 "	Malarial.
3	++	2	1	10 "	"
4	++	3	1	3 "	"
5	++	2	O	4 "	Enteric-like.
6	++	$1\frac{1}{2}$	1	2 "	"
7	++	$1\frac{1}{2}$	?	1 month	Malarial.
8	++	P	?	27 days	"
9	+	O	..	3rd week	Enteric-like.
10	++	$2\frac{1}{2}$	+	$1\frac{1}{2}$	Malarial.
11	+-	2	+	?	"
12	++	4	$1\frac{1}{2}$	6 months	Enteric-like.
13	++	5	+	6 "	"
14	+-	6	+	$1\frac{1}{2}$ years	Malarial.
15	++	$1\frac{1}{2}$	+	$1\frac{1}{2}$ "	"
16	++	$1\frac{1}{2}$	+	3rd week	Enteric-like.
17	+-	P	?	3rd "	"
18	+	P	+	4 months	"
19	+	P	O	1 month	Insidious.
20	+	4	1	6 months	Enteric-like.
21	T -	4	+	1 year ?	Remittent-intermittent.
22	++	6	+	3 months	Enteric-like.
23	++	4	2	2 "	"
24	++	1	+	$1\frac{1}{2}$ "	Malarial.
25	++	$1\frac{1}{2}$	$\frac{1}{2}$	2 "	"
26	+-	3	+	4 "	"
27	++	3	1	4 "	Enteric-like.
28	++	1	+	1 month	"
29	+-	$3\frac{1}{2}$	1	2 months	"
30	++	4	+	1 year	Malarial.
31	+-	$3\frac{1}{2}$	1	8 months	"
32	++	$4\frac{1}{2}$	$1\frac{1}{2}$	1 year	? Enteric-like.
33	+-	2	+	21 days	? Insidious.
34	+	4	+	2 months	Malarial.
35	++	5	+	?	"
36	++	7	2	8 "	"
37	++	1	P	$2\frac{1}{2}$ "	"
38	++	++	+	?	Enteric-like.
39	++	+	+	?	?
40	+-	..	..	?	?
41	++	+	+	?	?
42	-	+	+	3 months	?

TABLE III  
'Aldehyde-doubtful' cases of kala-azar

Serial number	C. F. test	Spleen, inches	Liver, inches	Duration of illness	Type of onset
1	+ ±	+	+	1 month	Enteric-like.
2	- -	4	P	4 months	"
3	++	2	P	$1\frac{1}{2}$ "	Malarial (KA + PT).
4	+-	2	1	2 "	Malarial.
5	+ ±	$1\frac{1}{2}$	+	? 1 year	Enteric-like.
6	+ ±	3	+	? 5 years	Malarial.
7	+ ±	++	+	..	Relapsed after M&B 800.
8	+ ±	++	+	..	"
9	++	2	P	5 months	Malarial.
10	± -	2	1	1 month	"
11	++	2	O	? 1 year	Enteric-like.
12	++	5	+	4 months	"
13	+ ±	1	P	? 10 months	Enteric-like.
14	+ ±	+	+	?	Malarial.
15	+ ±	$1\frac{1}{2}$	+	1 month	Enteric-like.
16	+-	$1\frac{1}{2}$	$\frac{1}{2}$	3 months	"
17	++	2	1	4 "	"
18	++	5	$1\frac{1}{2}$	2 "	"
19	+	P	P	1 month	"
20	++	2	1	5 months	"
21	++	?	?	? $1\frac{1}{2}$ months	? Cancrum oris +.
22	+ ±	4	1	3 months	Malarial.
23	+ ±	$1\frac{1}{2}$	1	4 "	Enteric-like.
24	+ ..	5	+	6 "	"
25	Neg.	5	+	7 "	"
26	+ ..	O	O	3 "	'Had treatment. 3 months back.'
27	+	5	2	3 "	Enteric-like.
28	+	1	+	$3\frac{1}{2}$ "	"
29	+ ±	+	+	..	"
30	++	3	+	$3\frac{1}{2}$ "	Enteric-like.
31	++	4	+	? 2 years	"
32	+-	4	+	7 months	"
33	+ ±	6	+	1 year	"
34	+-	6	2	? 6 days	"
35	++	+	+	3 months	Malarial.
36	++	$2\frac{1}{2}$	+	9 "	"
37	++	2	1	3 "	"
38	+-	2	P	? 1 year	"
39	+-	6	1	1 "	"
40	+ T	2	+	6 months	"
41	++	3	+	7 "	"
42	± -	3	1	$1\frac{1}{2}$ "	Enteric-like. Had 1 injection.
43	++	4	2	6 "	"
44	++	5	$2\frac{1}{2}$	6 "	Malarial. "
45	++	$1\frac{1}{2}$	$\frac{1}{2}$	? 2 years	KA and PT malarial.
46	+-	+	+	?	"
47	++	+	+	5 months	Enteric-like.
48	+-	$1\frac{1}{2}$	1	$1\frac{1}{2}$ "	Double intermittent.
49	++	4	$1\frac{1}{2}$	3 "	Cont. pyrexia with rigors.
50	+-	$1\frac{1}{2}$	$2\frac{1}{2}$	5 "	Malarial.
51	+-	3	1	7 "	Enteric-like.
52	+-	$2\frac{1}{2}$	$2\frac{1}{2}$	? 3 weeks	Malarial.
53	+ ±	++	++	? 2 "	"
54	++	3	+	..	"
55	+ ±	$\frac{1}{2}$	?	1 year	Enteric-like
56	++	3	+	3 months	"

Abbreviations used:—O=not enlarged; P=just palpable on inspiration; KA=kala-azar; PT=pulmonary tuberculosis.

puncture in kala-azar is not more than 89 per cent (Napier, Sen Gupta and Sen, 1942). The conclusion is justified that in the diagnosis of kala-azar in the very early stages, this test is superior to all other serum tests and that there is probably a better chance of obtaining a positive evidence of kala-azar by this test than by sternal puncture. In the group of 'aldehyde-doubtful' cases of kala-azar, the percentage of positives is over 94 per cent and the remarks concerning the very early cases are equally applicable.

*The value of the test in the cases giving a positive reaction with the aldehyde test.*—Napier was of the opinion that in the absence of obvious pulmonary tuberculosis or leprosy, a fully positive aldehyde test may be taken as indicating kala-azar in the endemic areas in India, where trypanosomiasis and bilharziasis do not exist. He did not find more than a dozen instances of positive reaction in cases other than kala-azar in his experience of over 20,000 tests. Recent experience indicates that the false positive aldehyde is not so very uncommon particularly among 'sick destitutes'. During the present investigation, 7 cases were encountered in which a positive reaction was obtained with the aldehyde test in the absence of kala-azar, 2 cases amongst famine-stricken destitutes, 2 cases of splenomegaly with anaemia, one case each of carcinoma of the stomach, cirrhosis of the liver and mixed benign tertian and malignant tertian infection. In these cases with splenomegaly and anaemia, and in the destitute cases, the subsequent history and findings ruled out kala-azar. In the 3 of these 7 cases, the diagnosis was based on the clinical features and there was no evidence of leishmaniasis. In 5 of these 7 cases the complement-fixation test was negative, in one case with splenomegaly with anaemia the serum was anti-complementary and in the case of cirrhosis of liver with ascites, and jaundice, the complement-fixation test was doubtful. On the other hand, of the aldehyde-positive kala-azar cases the complement-fixation test gave a doubtful reaction in about 6 per cent and a negative reaction in about one per cent of the cases. It would thus appear reasonable to do a complement-fixation test in aldehyde-positive cases too so that, if there is a disagreement in the results of these two tests, splenic or sternal puncture and culture for leishmania should be done before a case is labelled kala-azar. The proportion of cases showing false positive reaction with the aldehyde test and a negative reaction with the complement-fixation test is however very small.

*The effect of specific treatment on the complement-fixation test for kala-azar.*—In 63 cases the test was repeated after the completion of treatment, using both 1 : 25 and 1 : 100 dilutions of serum.

It was found that in 31 cases the reaction had become completely negative. The initial reaction in this group was 'positive' in 27 cases, 'doubtful' in 2, 'negative' in one and 'anti-complementary' in one case. In 24 cases

the reaction was found to be 'doubtful' after treatment. The initial reaction in this group was positive in 22, doubtful in one, anti-complementary in one. In 6 cases there was decrease in the degree of positive reaction, i.e. a positive reaction in both 1 : 25 and 1 : 100 dilutions, turned into positive reaction in 1 : 25 and negative or doubtful reaction in 1 : 100 dilution of serum. In 2 cases, there was no appreciable change in the serum reaction.

Thus in most cases, the complement-fixation reaction disappeared or the titre was reduced after treatment. The question whether this test can provide us with a test for complete cure of kala-azar is under investigation at present.

In this connection mention should be made of the fact that if the complement-fixation test is carried out for the first time after the patient has had a number of injections of specific drug for kala-azar, there is some chance of the serum giving a doubtful or even a negative reaction.

*High anti-complementary titre.*—Eight out of the 169 aldehyde positive sera were found to be anti-complementary, and thus no opinion could be formed about their complement-fixation reaction with the antigen used. These 8 cases have been excluded from table I. Bearing in mind the fact that the serum was used in 1 : 25 dilution, 8 out of 169, i.e. approximately 1 in 20, is a very high proportion. Usually during routine work about 1 in 50 sera when diluted 1 : 5 as in WR are found to be anti-complementary. This finding confirms the opinion expressed in a previous communication (Greval, Sen Gupta and Napier, 1939) that the limit of anti-complementary activity of human serum is reached in some cases of kala-azar. It is also significant that these 8 cases belong to the aldehyde-positive group and that none of the aldehyde doubtful or negative sera proved anti-complementary. We know that the positive reaction in the aldehyde test is caused by marked increase in the euglobulin fraction of the serum. It is possible that the changes in the globulin fraction is in some way related to the anti-complementary activity of the serum.

### Summary

1. The results of complement-fixation test in 920 cases done according to the technique described by Greval, Sen Gupta and Napier (1939) using an antigen prepared according to Witebsky, Klingenstein and Kuhn method from Kedrowsky's bacillus are reported.

2. It has been found that a positive reaction is obtained in 93 per cent, a doubtful reaction in 6 per cent and a negative reaction in one per cent of all cases of kala-azar.

3. In 99 per cent of all cases likely to be considered in the differential diagnosis of kala-azar a negative reaction is obtained. In one per cent a doubtful reaction may be obtained.

4. A positive reaction is obtained in a small proportion of obvious cases of chronic pulmonary tuberculosis. But this fact does not prove a serious handicap to the usefulness of the test

because such cases are readily excluded by their clinical features.

5. On comparison with the results obtained with the original WKK antigen it is found that the antigen prepared from Kedrowsky's bacillus is somewhat inferior, because it gives a positive reaction in a smaller proportion of cases. It is probable that with the antigen prepared locally from the human tubercle bacillus, better results will be obtained.

6. In the diagnosis of early cases of kala-azar, this test provides a method of laboratory diagnosis at a stage when all others except a sternal puncture (which has slightly lesser chances of being positive) are negative. In several cases the positive reaction was obtained within 3 weeks of onset. In a larger number of early cases showing slight or no enlargement of the spleen, a positive reaction was obtained; there was no marked enlargement of the liver in these cases.

7. In the aldehyde-positive cases this test serves to distinguish the non-kala-azar cases giving a positive aldehyde test. The proportion of such cases is however very small.

8. Specific treatment of kala-azar causes the reaction to become negative or produces a definite lowering of the degree of complement fixation.

#### Conclusion

The complement-fixation test done according to the technique described by Greval, Sen Gupta and Napier, using either the original WKK antigen or an antigen prepared from certain acid-fast bacilli according to WKK method, provides a diagnostic test of great value in kala-azar. The test is positive at a stage when all other serum tests are negative. The chances of obtaining a positive indication of kala-azar are probably greater with this test than with the examination of sternal puncture smear for leishmania.

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## THE QUALITY OF INDIAN-MADE SYNTHETIC DRUGS. II

### EXAMINATION OF IODOCHLORHYDROXY-QUINOLINE (ENTEROVIOFORM) OF INDIAN MANUFACTURE

#### Laboratory Study

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#### Clinical Study

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In the course of a comprehensive survey of the chemotherapy of amœbiasis, Leake (1932) studied the properties of iodochlorhydroxyquinoline (enterovioform or vioform, N.N.R.) in comparison to chiniofon, N.N.R. (sodium iodoxyquinoline sulphonate) and certain other derivatives of hydroxyquinoline from the standpoint of oral toxicity in guinea-pigs and cats, amœbicidal action *in vitro*, and balantidicidal effect in naturally infested guinea-pigs. His observations, later confirmed in a joint report by David, Johnstone, Reed and Leake (1933), definitely indicated that this compound was an effective anti-dysenteric remedy with a superior curative rate in non-toxic doses over chiniofon (trade marked names: 'Yatren', 'Anayodin', etc.). The compound was marketed for the first time by the Ciba Company and has since earned a fair amount of popularity particularly in the treatment of refractory cases of chronic amœbic infections. In India, this synthetic drug was already in demand when the war broke out, and the gradually developing shortage of emetine coupled with the newer knowledge about its toxicity to the myocardium made the medical profession turn to this and similar other synthetic anti-dysenteric remedies, e.g. carbarsone, etc., more and more enthusiastically. The supply of this drug was entirely imported until recently, when a few Indian manufacturers have synthesized the compound. This laboratory had the opportunity of examining most of these brands even before these were released into the market, and the present paper embodies a collaborative study of the laboratory and clinical evaluation of Indian-made 'Vioform' powders and tablets.

#### Experimental

A. Analytical data. As in case of the chemical examination of carbarsone (Mukerji *et al.*, 1944), the object of this study was to compare critically the Indian-made compound with iodochlorhydroxyquinoline manufactured and marketed by Ciba Company. All the

tests recommended by the N.N.R., 1941, were therefore followed side by side with the standard product of Ciba Company.

(i) *Physical characters and solubility.*—The Indian-made 'Vioform' is a greyish-yellow powder, having a very faint aromatic odour, almost insoluble in water, sparingly soluble in alcohol, soluble in hot glacial acetic acid. These tests compare favourably with the Ciba 'Vioform'.

'Vioform' powders in table I and for 'Vioform' tablets in table II.

A glance at the tables will indicate that in the case of the Indian-made 'Vioform' powders (table I), the melting-points of almost all the samples examined come close to or within the N.N.R. range. The percentage of iodine in all the samples is within the N.N.R. standards but the percentage of chlorine in all the cases (with the exception of no. 9) is invariably above the

TABLE I  
*Analysis of iodochlorhydroxyquinoline powders*

Number	Name	Sender	Melting-point in °C.	Percentage of iodine	Percentage of chlorine
1	Ambisyl .. ..	S. P. P.	176	41.83	14.30
2	Enterovioform .. ..	I. R. I.	174	39.26	16.83
3	Quinambicide .. ..	B. R. I.	176	40.06	15.16
4	Vioform .. ..	S. P. P.	178	40.63	16.20
5	Quinambicide .. ..	B. R. I.	178	40.73	15.20
6	Enterovioform .. ..	I. R. I.	176.5	40.42	17.06
7	Do. .. ..	I. R. I.	177	38.66	16.40
8	Enterochin .. ..	I. R. I.	178	38.83	15.91
9	Iodochloroxyquinoline .. ..	P. C. P. W.	172	39.76	10.99
10	Enterovioform crystallized from 'Ciba' brand tablets.		177.5	40.93	15.10
	N.N.R. standard .. ..		178-180	37.5-41.5	11.5-12.2

TABLE II  
*Analysis of iodochloroxyquinoline tablets*

Number	Name	Sender	* Iodine in gm. per tablet	* Chlorine in gm. per tablet
1	Quinambicide .. ..	B. R. I.	0.103	0.041
2	Iodochloroxyquinoline .. ..	M. S. I. D.	0.093	0.041
3	Quinambicide .. ..	B. R. I.	0.112	0.041
4	Iodochloroxyquinoline .. ..	M. S. I. D.	0.115	0.038
5	Iodochloroxyquinoline .. ..	M. S. I. D.	0.080	0.036
6	Quinambicide .. ..	B. R. I.	0.076	0.062
7	Iodochloroxyquinoline .. ..	M. S. I. D.	0.076	0.041
8	Iodochloroxyquinoline .. ..	M. S. I. D.	0.080	0.024
9	Iodochloroxyquinoline .. ..	M. S. I. D.	0.085	0.045
10	Iodochloroxyquinoline .. ..	M. S. I. D.	0.086	0.043
11	Iodochloroxyquinoline .. ..	M. S. I. D.	0.088	0.043
12	Quinambicide .. ..	B. R. I.	0.099	0.043
13	Iodochloroxyquinoline .. ..	M. S. I. D.	0.094	0.042
14	Iodochloroxyquinoline .. ..	M. S. I. D.	0.106	0.043
15	Iodochloroxyquinoline .. ..	M. S. I. D.	0.094	0.048
16	Enterovioform, 'Ciba' brand	M. S. I. D.	0.080	0.038
	N.N.R. standard .. ..		(37.5% to 41.5%) 0.0937 to 0.1037	(11.5% to 12.2%) 0.0287 to 0.0305

\* Claim in each of the above sample = 0.25 g. enterovioform per tablet.

(ii) *Chemical analysis.*—Pal and Guha (1943) have already shown that the N.N.R. (Amer. Med. Assoc., 1941) method for the estimation of iodochlorhydroxyquinoline requires modification in certain important respects in order to get dependable results. In this investigation, the modified method of estimation was therefore followed. The results are shown, for

N.N.R. specifications. It has not yet been possible for us to explain this difference. Crystals obtained from 'Ciba' brand tablets of iodochlorhydroxyquinoline (as 'Ciba' brand powder is not available in India), after repeated recrystallization from hot glacial acetic acid, were analysed several times for chlorine content, employing the same method as previously. In

these cases also, the percentage of chlorine was found to be higher than the N.N.R. figure. As our study is essentially a comparative one, with the 'Ciba' product as the 'standard', we have only recorded this observation without attempting to offer any satisfactory explanation.

In the case of iodochlorhydroxyquinoline tablets (table II), we have determined the quantities of iodine and chlorine present in the average weight of a tablet claimed to contain 0.25 g. of 'enterovioform' per tablet. When these iodine and chlorine contents are converted to their respective percentages, taking 0.25 g. of enterovioform to be constant in every case, chlorine content is found to be higher than, but iodine content almost within the limit of, the N.N.R. specification. This agrees closely with the analytical figures of the 'Ciba' brand tablets, and therefore the conclusion seems justifiable, as far as laboratory data are concerned, that the locally synthesized brands of 'enterovioform' are almost identical with the 'Ciba' compound as available for sale in the Indian market.

*B. Clinical trials.* These were conducted in hospitalized patients with proved cases of vegetative and/or cystic forms of *E. histolytica* present in stool examination at the time of admission. A regular follow-up was made in every case for a period varying from 3 to 6 months. No case was pronounced as cured where repeated stool examinations were not made by sigmoidoscopic control before and after the treatment.

Twenty-four cases of human amoebiasis were so far treated with two locally synthesized brands of iodochlorhydroxyquinoline tablets in doses of 0.25 g. thrice daily for 10 days. Of these, 19 patients were *completely cured*. Three cases showed clinical improvement but stool examination gave positive findings and another two had inconclusive results. In spite of the comparatively high chlorine content as determined by us (over N.N.R. standard), gastro-intestinal irritation, referable directly to the effect of the drug in the dosage employed, was not complained of. The possibility of iodism in sensitive individuals with a compound of this type containing so much iodine was kept in view, but no symptoms pointing to this condition were noticed in any case.

David *et al.* (1933) tried the drug in human amoebiasis in the same dosage and under similar controlled conditions in America. They reported that out of 47 unselected cases, 38 cases were cured; in 6, recurrences were found in contacts and 3 patients could not be followed. This is a parallel record to what has been obtained by us with locally-made 'Enterovioform'.

#### Comments

Judging from the evidence at our disposal (chemical analysis and clinical trials), it seems justifiable to state that the locally synthesized

iodochlorhydroxyquinoline compares very favourably with the 'Ciba' brand 'Vioform', and may be considered as a worth while equivalent of the imported product. None of the brands agree with the standards of chlorine content mentioned in N.N.R., but this is offset by the fact that the 'Ciba' tablet also gives a higher chlorine content by the same method of analysis. In any event, it may be recorded that the few brands of iodochlorhydroxyquinoline synthesized in India and examined by us are more or less equivalent to the 'Ciba' product and can be accepted by the medical profession as suitable for wider clinical trial in amoebiasis cases. The median toxicity in guinea-pigs on single oral administration with one brand of the local product came to about 180 mg./kg. (observation for 3 days), which is more or less similar to the toxicity (200 mg./kg. kills 13/20 pigs in 4 days) obtained by David *et al.* (*loc. cit.*). There is therefore no cause for anxiety in giving trial to any of the Indian products.

#### Summary

Indian-made iodochlorhydroxyquinoline differs slightly in chlorine content from the standard product of the same name in N.N.R. 1941, but agrees closely in melting-point, physical characteristics, solubility, iodine and chlorine percentages with the 'Ciba' brand 'Enterovioform'. Its toxicity (one brand only tested) is within safe limits in therapeutic dosages. In clinical trials in controlled cases of amoebiasis in hospitalized patients, it has given comparable satisfactory results.

The Indian-made synthetic product is therefore likely to be of the proper standard, and wider clinical trial to these brands can be given by the Indian medical profession in suitable cases without any risk to their patients when employed in therapeutic doses.

#### Acknowledgment

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## ANACIDITY IN GASTRIC CANCER

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THE problem of gastric cancer is most discouraging. The prodigious efforts expended by clinicians, as well as research workers in the study of the malignant disease, probably has had less effect on the mortality of gastric cancer than on that of any other of the common types of carcinoma. The gloomy aspect of gastric cancer has been vividly emphasized by Schindler (1941) while discussing the necessity of early diagnosis of the disease. He said 'If every patient with gastric carcinoma entered the best surgical clinic in the world 95 per cent would still remain uncured and approximately 90 per cent would be dead of the disease within 18 months. On the average, not more than 2 per cent of all gastric carcinoma cases which enter a clinic or a hospital can be cured'. This much for the state of affairs in most civilized countries where medical aid is obtainable at its best. If such is the hopeless outlook in countries where skill in diagnosis and treatment of cancer has been very highly developed, the outlook is still darker in our country where adequate medical aid is non-existent except in few large cities.

The most evident reason for such discouraging failures is that the majority of cases seek medical advice at a very late period. The patients who have mild initial symptoms such as lack of appetite, slight loss of weight or a little epigastric distress are unwilling to undergo time consuming and expensive medical examinations. It is also true that gastric lesions are prone to set up disturbances in the general metabolism of the body more rapidly than many other types of carcinoma. This brings about multiple complications into play much too soon. All such complications have their primary origin in the digestive disturbances which in their turn originate chiefly from the hypo-acidity or a complete anacidity of gastric secretion in the cancer of the stomach. Thus anacidity or hypo-acidity in gastric cancer is a matter of great importance and as such has been a matter of extensive investigation for the last half century. Many research workers probably believed that if a correct mechanism of gastric dysfunction in cancer could be understood, steps could be taken to restore normal gastric secretion in patients with carcinoma of the stomach and thus probably increase the survival period or at least help the surgeon in dealing with a malignant lesion without many nutritional complications.

The first study of gastric acidity in cancer of the stomach was attributed to Golding Bird by Ewald (1893) from whom the quotations have been copied by subsequent workers. These workers found a diminished acidity throughout

the duration of the disease although study of the original reports leaves considerable doubts as to the real state of affairs.

Van den Velden (1897) was the first to make any purposeful study of gastric secretion in cancer of the stomach. He examined the fluid drawn off in cases of gastritis and found that in those patients who had cancer of the stomach, free HCl was absent. Riegel (1908) and others supported their findings. Miehe who wrote in 1890 disagreed with the claims of the above workers. On the basis of 5 cases of cancer of the stomach seen at autopsy, he was able to demonstrate free HCl by the colour reaction after an Ewald meal. He, however, agreed that HCl was usually but not always absent and practically always diminished. Ewald (*loc. cit.*) on the other hand thought that HCl was always absent except in very small early cancers or in cancer on an ulcer basis. Oppeler's (1895) studies were among the most thorough of the earlier ones. He states that with intact motor function (without pyloric obstruction) acid is usually absent, but with disturbances of motor function (early pyloric cancer), acid is present in strong concentrations. He found an absence of HCl in advanced ulcerated growth. Einhorn (1906) who supported the previous views was the first to show that sometimes acid was present in concentrations more than normal. Riegel (1908) later departed from his earlier opinion that the acid is invariably absent and admitted that it may be present in very early cases. Cohnheim (1908), Hayem and Lion (1913) and Boas (1911) agreed with earlier workers.

Brown (1927) reported anacidity in 75 per cent of the cases of the carcinoma of the stomach. Pollard and Bloomfield (1930) have shown that the gastric curve after histamine meal has a diagnostic value in the cancer of the stomach. They have shown that low free acidity and low volume was found in cases of cancer of the stomach, while in duodenal ulcers the values were usually high. These authors found anacidity in 69 per cent of cases even after histamine. Shay and Schloss (1934) reported an incidence of 44.4 per cent.

Comfort and Vanzant (1934) published data which indicated that there is a relationship between the size of the lesion and the incidence of anacidity. They found that in cases of gastric cancer measuring 3 cm. or less in diameter, the mean free acidity and the incidence of anacidity was practically the same as for normal persons. As the size of the lesion increased, the mean free acidity became lower and the incidence of anacidity higher. Anacidity occurred in 40 per cent of cases in which the average diameter was 1.3 cm. This was 11 per cent less than the expected incidence for a similar normal group; with lesions averaging 3.16 cm., the frequency of anacidity increased to 28 per cent which was 8 per cent more than the expected incidence for a similar normal group. These findings they

explained on the basis of progressive gastritis which usually accompanied gastric malignancy.

Hurst (1936) believed that achlorhydria in cancer of the stomach was really due to chronic gastritis which was present before the growth developed, the growth being the result of malignant degeneration of the chronically inflamed mucous membrane. He stated that in no case was free acid found in the stomach at a time when a growth was first recognized, which disappeared at a later date. However, such cases have been reported by Bockus, Bank and Willard (1932), Robertson (1935) and Comfort, Butsch and Eusterman (1937). Shay and Schloss (*loc. cit.*) have reported a patient in whom there was not only free acid but also a normal secretory response at the time the gastric lesion was first found, and in whom complete anacidity developed later. Comfort, Butsch and Eusterman (*loc. cit.*) carried out gastric analysis in 79 cases before and after the development of carcinoma of the stomach. They found secretory activity below normal before the development of cancer. After an average period of six years, the time between the first gastric analysis and the development of cancer, they found the incidence of anacidity had increased from 38 to 64.6 per cent. These facts support the belief that probably the gastric anacidity was not the effect of the malignant growth but a cause leading to such growth. It is also interesting to note the finding that the incidence of anacidity in patients with pernicious anæmia is even higher than that in the patients with carcinoma of the stomach, and that the incidence of benign and malignant neoplasms of the stomach is greater among patients with pernicious anæmia than among comparable age and sex groups in the population at large (Rhoads, 1941).

During the last three years it had been possible at this hospital to study a few cases of cancer of the stomach for their gastric secretion, and it was thought worth while to scrutinize the data in the light of above observations, and report the findings.

### Experimental

The gastric analysis is done as a routine investigation on the patients in whom some gastric lesion is suspected clinically or radiologically. 7 per cent alcohol is used as a test meal. In the table are given the free and total acidity in cancer cases. Interpretation of the results is done on the basis of the findings by Mangalik and others (1942).

### Discussion

(a) *Frequency of anacidity.*—From the table it could be seen that out of 24 cases of carcinoma of the stomach, 12 cases presented complete anacidity; in 9 cases the acidity is greatly reduced and in 3 cases it was rather high (nos. 1, 12 and 18). Thus in 87.5 per cent of the cases, the gastric secretion is diminished. No correlation could be established between the free

acidity and the combined acidity except that the combined acid was not diminished even when there was anacidity. According to Hollander (1934) and Mitchell (1931) the buffer substances which were manifested on titration as 'combined acidity' increased when the free acidity diminished. This observation was borne out in the present observations only in part.

(b) *Site of tumour formation and acidity.*—If one scrutinized the data on the basis of site of tumour formation, the table showed that, out of 24 cases, 20 had their lesion at the pyloric end, and the majority of these cases showed reduced gastric acidity. Out of the remaining 4 cases, one (no. 3) was at the fundus end while in the other 3 the actual site of tumour could not be located since no surgical specimen was available. Even in the case (no. 3) where the tumour was in the fundus area, complete anacidity was observed after test meal. Thus it appeared probable that the spread of the tumour as well as the site were deciding factors in determining the acid secretion.

(c) *Spread of lesion and acidity.*—Comfort and Vanzart (*loc. cit.*) have shown a close relationship between the size of the tumour and anacidity. This observation was only partly borne out in the present study. In general, there appeared to be some relation between the spread of the lesion and anacidity. This was however logical, because the greater the spread, the greater was the number of secreting cells destroyed. But in cases nos. 5 and 14 where the lesions were 60 sq. cm. and 100 sq. cm. respectively, the acidity was higher than in cases nos. 4 and 23 where lesions were comparatively small. In such cases there must be some other factor or factors governing the acidity.

(d) *Duration of disease and acidity.*—In cases nos. 2, 14 and 15, one could see that the duration of the disease was above two years. In these cases although the lesions were fairly large, free hydrochloric acid was present in measurable amounts. This finding could be explained on the supposition that probably these tumours originated from previous ulcers. Ewald (*loc. cit.*) has also said that in cases of carcinoma of the stomach which originated from ulcers, free acid was always present.

From the above discussion it is clear that gastric anacidity is a usual finding in carcinoma of the stomach. This has been found by many previous workers cited above; but it is very difficult to say which of the factors discussed above bring about such a change.

According to Babkin (1938) the physiology of gastric secretion is under the control of two phases: (1) a hormonal phase which is mainly governed by the parasympathetic stimulation of the vagus nerve and in which histamine plays an important rôle and (2) a chemical phase in which numerous members participate to carry out the normal physiological functions. Evidence is slowly accumulating that the cause of gastric anacidity or hypo-acidity in cancer might be found in disturbance in this phase.

TABLE

*Gastric acidity in patients with carcinoma of the stomach*  
(in terms of c.cm. of N/10 NaOH per 100 c.cm. of juice)

Serial number	Case number	Age	Sex	Grade histological	Spread of lesion, sq. cm.	Duration of disease	Fasting volume in c.cm.	FASTING		½ HOUR		1 HOUR		2 HOUR		1 HOUR		1½ HOURS	
								Free	Total	Free	Total	Free	Total	Free	Total	Free	Total	Free	Total
1	447	45	F.	III P	20	2 years	95	164	188	30	46	54	76	102	128	90	128	124	160
2	538	38	M.	IV P	135	2 "	88	20	28	4	12	6	14	8	20	10	18	16	26
3	680	74	F.	III	93	3 months	60	36	68	0	10	0	14	0	16	0	20	0	16
4	726	53	F.	III P	40	6 "	90	16	38	16	24	10	20	10	18	10	27	10	22
5	756	50	F.	II	60	6 "	18	56	76	10	22	32	40	36	50	24	36	36	40
6	1241	55	M.	III P	80	1 year	2.8	0	12	0	12	10	25	0	50	0	54	..	40
7	1804	60	M.	II P	75	2 years	35	0	14	0	14	0	18	6	8	0	8	0	..
8	2029	60	M.	II P	8	3 "	20	46	98	28	36	30	40	34	44	34	44	30	44
9	2060	50	F.	II P	70	4 months	18	0	16	0	8	0	6	0	6	0	6	0	8
10	2183	55	F.	III P	70	2 "	18	0	20	6	12	4	15	6	14	4	18	4	16
11	2446	67	F.	GEL P	100	7 "	32	52	18	44	32	26	26	72	26	22	48	18	18
12	2572	50	M.	II P	8	1 year	14	0	64	0	56	15	66	15	80	12	44	8	58
13	2863	55	M.	— P	80	1 "	6	38	10	4	4	22	22	38	25	22	44	18	18
14	2888	51	M.	GEL	100	3 years	20	20	74	18	70	4	70	4	86	14	92	..	86
15	3361	43	M.	GEL P	80	5 "	25	10	42	30	44	24	18	20	38	26	26	..	58
16	3655	50	M.	II P	20	25 days	17	0	34	0	56	..	54	0	48	0	58	..	58
17	3838	49	M.	II P	110	1 year	11	38	12	28	4	..	10	58	10	16	12	..	..
18	4024	47	M.	II	..	4 months	1.5	16	66	16	40	20	40	24	70	24	30	30	30
19	4209	60	M.	II P	77	5 "	9.5	0	26	0	26	0	26	0	36	0	36	0	38
20	4364	42	F.	GEL P	79	1 year	20	0	26	0	8	0	12	0	10	0	12	..	8
21	4577	65	M.	II P	120	2½ months	20	0	38	0	16	0	20	0	24	0	30	0	..
22	4597	35	M.	III P	58	4 "	25	0	8	0	8	0	15	0	12	0	10	..	12
23	4653	67	M.	II P	20	6 "	6	0	12	0	16	0	20	0	20	0	25	0	..
24	5456	43	M.	II P	120	4 "	20	0	30	0	32	0	40	0	44	0	30	0	44

P=Pyloric region involved.

The chemical phase in gastric secretion has a triple mechanism: (1) the pyloric chemical phase, (2) the secretagogue effect of some food substances and some products of digestion obtained from the small intestine and (3) the direct effect of hypoglycæmia and of certain other substances in the circulating blood on the vagal secretory centre.

Out of these three mechanisms, the effect of only the first and the third need be considered

when the gastric anacidity in cancer is to be understood. The secretagogue effect of digested foodstuffs on the small intestine is a factor which would influence the gastric acidity curve, rather than the initial level; even so its effect may be presumed to be very small.

The most important factor in the chemical phase of gastric secretion is therefore the pyloric phase. The pyloric mucosa is concerned in the elaboration of hormone 'gastrin' (Komorov,

1938) which is distinct from both histamine or choline. This hormone is supposed to control the normal gastric secretion. The exact mechanism of its action is not clearly understood, but it is almost certain that 'gastrin' stimulates the parietal cells preferentially, since the stimulated juice is rich in hydrochloric acid and poor in pepsin. In the case of carcinoma of the stomach—which is usually at the pyloric end—it is likely that the mucosa has undergone an atrophy due to accompanying gastritis, and that the elaboration of gastrin is probably decreased. The decreased production of gastrin would decrease the stimulation of parietal cells, and less acid would be secreted. This possibility also seems likely because the total volume of secretion, which is produced mainly by the parietal cells, is also decreased in cancer of the stomach. However, a likelihood of the destruction of parietal cells by invading tumour cannot be ruled out.

The inhibitory effect on gastric secretion of insulin and other substances when circulating in the blood is well known [Babkin (*loc. cit.*)]. But no experimental evidence is on record which shows that such substances are found in large amount in the blood of patients with carcinoma of the stomach.

Another possibility is the elaboration of some substance by the cancerous tissue which would act as gastric depressant. Recently experimental evidence is forthcoming (Brunschwig *et al.*, 1941) which shows that in cases of carcinoma of the stomach, the gastric juice contains a substance which reduces gastric secretions when injected intravenously in dogs. A similar substance was isolated some time ago from the stomach of persons suffering from pernicious anæmia (Brunschwig *et al.*, 1939). These investigations have, however, helped to clear up the problem of gastric anacidity only to a certain extent. The identity of the substance which causes depression in acid secretion is not yet established. It is likely that the gastric depressants in pernicious anæmia and cancer of the stomach may be identical. This is made more likely by the finding that in the majority of cases with cancer of the stomach a history of pernicious anæmia is found. Ivy and Gray (1937) believes that the gastric depressant is probably the hormone 'enterogastrone' identified by himself and his collaborators from the duodenum, which might probably be formed by the pyloric mucosa in the presence of cancer. Brunschwig and others (*loc. cit.*) on the other hand argue that the enterogastrone could not be elaborated by the stomach mucosa, and that the gastric inhibitor found by them was distinct from it. Whether enterogastrone is identical with the inhibitory principle that was discovered by Brunschwig in patients with cancer of the stomach, or whether the latter is identical with that found in pernicious anæmia, will remain uncertain until these substances can be chemically isolated; and till then, little progress can be

made in clarifying the problem of gastric anacidity in cancer.

### Conclusion

1. Twenty-four cases of proved cancer of the stomach have been studied for their gastric secretion after an alcohol test meal.

2. Out of 24 cases, 12 cases presented complete anacidity and in 9 cases the acid secretion was greatly reduced. In 3 cases acid values were rather high.

3. The data have been scrutinized in relation to site of tumour formation, the spread of tumour and the duration of the disease. It is believed that all these factors contribute towards the resultant anacidity or hypo-acidity in cancer.

4. The chemical phase of gastric anacidity in cancer is discussed.

The author has great pleasure in thanking his colleagues at this hospital without whose co-operation the study would not have been possible.

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## A CASE OF MILIARY TUBERCULOSIS OF SEROUS MEMBRANES WITH A NON-TUBERCULOUS BRAIN ABSCESS

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THIS note describes a case in which miliary tuberculosis of serous membranes without any tuberculosis of underlying organs was associated with a non-tuberculous brain abscess.

**11th September, 1942.**—A Sikh soldier, aged 22 years, of average health and development, was admitted into hospital for midday fever, general malaise, and headache of 12 days' duration. He also had throaty cough without expectoration for a week. He had had no illness prior to this, and had stood up to the army life under active service conditions. Family history showed good health and long lives, with no suspicion of tuberculosis.

On admission he had a temperature of 101.4°F., pulse 98, respiration 24; throat congested, few scattered râles in both lungs; spleen—one finger palpable. Blood negative for malaria, and sputum showing no acid-fast bacilli. Urine and stool normal; blood culture sterile. Symptomatic treatment was given.

**16th September, 1942.**—Right-sided sero-fibrinous pleurisy developed; treatment on sanatorium principles instituted.

**29th September, 1942.**—Patient is generally much improved. The temperature, until now swinging between 98.4°F. and 102°F., has settled to normal by lysis. Sputum cultures on four occasions during the period showed no acid fast bacilli; microscopical examination of sputum for acid fast bacilli daily for three weeks was also negative.

**23rd October, 1942.**—X-ray showed a small effusion on right side of chest, thickened pleura over right middle and lower zones, and inter-lobar adhesions between the same lobes. The left pleura and both the lung fields were normal.

The general condition of the patient was satisfactory, and it was considered that the case, even if of tuberculous origin, was heading towards recovery.

**18th November, 1942.**—The soldier complained of 'being ill' and developed headache, malaise, and a temperature of 99°F. with a pulse rate of 88. Physical signs confined to those of thickened pleura on the right side. Blood examinations for malaria parasites, blood culture, routine urine examination, urine culture, agglutination for enteric, typhus, and undulant groups of fevers, were negative. Sputum was repeatedly negative for acid fast bacilli. Leucocyte count was 9,000 with 66 per cent neutrophils and 34 per cent lymphocytes.

The patient slowly became worse, the temperature ranging between 99°F. and 102°F., till 4th December, 1942, when he was quite toxic; leucocyte count 10,200 with 78 per cent neutrophils, 20 per cent lymphocytes, and 2 per cent monocytes. Occasional rhonchi and râles at bases of both lungs. Spleen just palpable; symptomatic treatment was given.

**14th December, 1942.**—Rather ill, more toxic, drowsy, answered questions reluctantly; stiffness of neck, generalized hyperæsthesia, tendon jerks brisk, vague abdominal tenderness with absence of superficial abdominal reflexes, plantar reflex was doubtful Babinski, Kernig's sign was positive, slight ptosis of left eye, some congestion of left inner canthus; leucocyte count

9,200 with 90 per cent neutrophils, 8 per cent lymphocytes, and 2 per cent monocytes.

The cerebro-spinal fluid was under tension, flowing at a rate of 4 to 5 drops per second, opalescent, and contained 400 cells per c.mm. Of these cells 87 per cent were pus cells, 4 per cent lymphocytes, 7 per cent endothelial, and 2 per cent red blood corpuscles. Sugar present in traces only and chloride was 620 mg. per 100 c.cm. An organism of the proteus group was grown on culturing the cerebro-spinal fluid and it was agglutinated by the patient's serum in a dilution of 1 in 50. A diagnosis of suppurative meningo-encephalitis was made at this stage.

**16th December, 1942.**—Sulphapyridine 4 tablets given as a first dose, and thereafter 2 tablets four hourly until 30 tablets were given in all, without any beneficial effect however.

**17th December, 1942.**—Patient unable to recognize friends, dysarthria, nearly deaf, has a right-sided supra-nuclear type of facial paralysis, right-sided hemiparesis; pupils react sluggishly to light; fundi oculi (examined with difficulty) showed bilateral papilloedema, neck rigid; bilateral positive Babinski.

**18th December, 1942.**—Generalized hyperæsthesia, incontinence of urine, blood pressure 115/76.

**19th December, 1942.**—Comatose; convulsions of right side of body, right facial paralysis; pupils nearly inactive, left eye has marked ptosis. General condition worse. Leucocytes 9,800 with 78 per cent neutrophils, 18 per cent lymphocytes, and 4 per cent monocytes.

**20th December, 1942.**—Cerebro-spinal fluid under increased pressure; cell count 600; chloride 600 mg. per 100 c.cm. Sugar—absent.

**21st December, 1942.**—Deep coma and incontinence of faeces. Signs of broncho-pneumonia in left lower lobe.

Thereafter he became progressively worse, the temperature rose as a terminal feature, and he died on 25th December, 1942.

**25th December, 1942.**—Autopsy performed on same day—within three hours of death; only relevant post-mortem and histological findings are given.

**Thorax.**—No free fluid in pleural cavities; both visceral and parietal pleura of both sides extensively covered with miliary tubercles, the process being most marked at the right base posteriorly; left apex entirely free while right apex had only few tubercles. Adhesions were marked along posterior borders of both lungs, the diaphragm, and a strong tag of adhesion was present on the sixth left rib in the axillary line.

The left lung showed inter-lobar adhesion; there was lobular consolidation in the lower half of the left lower lobe; it was terminal broncho-pneumonia without evidence of tuberculosis.

The right lung showed marked congestion of lower lobe but no evidence of tuberculosis.

**Histology.**—Sections from various parts of both lungs showed extensive miliary tuberculosis of the pleura, but no tuberculosis of the lung tissue. There were, however, collapse and broncho-pneumonia.

The bronchi showed uniform congestion of the mucosa down to the smallest branch; the hilar glands were slightly enlarged, discrete, and one gland showed caseation. Histological examination showed old tuberculosis of hilar glands, with giant cells, and in one gland macrophages with excess of brown pigment.

**Heart.**—Muscle was moderately firm and showed slight cloudy degeneration. There was no endocarditis or any ante-mortem thrombus.

### Abdomen

**Liver.**—Normal size but fatty and rather easily friable; a cluster of 20 to 30 white small seed-like bodies, apparently tubercles, covering about an inch square, and a small focus of necrosis close to the cluster present on the inferior surface of the left lobe. There was no other evidence of tuberculosis of the liver and even those noted above were apparently due to contiguous spread.

Sections showed the abscess to be non-tuberculous in nature but the cluster proved to be miliary tubercles.



*Peritoneum.*—Non-adherent tubercular peritonitis with very little free fluid. The stomach, intestines, pancreas, and the spleen were covered with miliary tubercles, but these are confined to the peritoneal coats only and the organs themselves showed no tuberculosis or any other abnormality. Histologically the peritoneum was covered with numerous miliary tubercles.

The abdominal lymph glands were apparently normal.

*Spleen.*—Twice normal size, perisplenitis at lower pole; cut surface showed moderate fibrosis; smear from cut surface showed no parasites or organisms.

*Brain and meninges.*—The dura was normal. There was a small amount of thick green pus under the arachnoid in the regions of the mid-brain and the upper left half of the pons. This pus was localized and had no apparent communication with the ventricles. The pia was inflamed on both sides, more so over the right island of Reil, the right occipital lobe and the upper third of the right post-central gyrus. There were a few miliary tubercles, confirmed histologically, on the pia-arachnoid in the right island of Reil. A small amount of thin gelatinous pus, confirmed microscopically, was present over the left cerebral hemisphere. The pia showed patchy inflammation in the upper half of the cerebellum.

The left cerebral hemisphere was concave in outline; a necrotic softening without any hæmorrhage or tuberculous process had affected the whole of the parietal and frontal lobes, the upper half of the temporal lobe, and the anterior half of the occipital lobe. The softening extended to within as little as half an inch of the surface in some places but there was no communication with the ventricles. From the necrotic area a proteus bacillus was grown on culture and it was similar to the one grown from cerebro-spinal fluid. Biochemically, microscopically, and it also agglutinated with the patient's serum in a dilution of 1 in 50. Unfortunately it was not possible to study the organism further. Histologically the abscess proved to be an acute non-tuberculous one; with complete necrosis of brain tissue.

In the right cerebrum there was slight but diffuse congestion of the white matter; in the mid-brain there was uniform pinking of the brain matter and slight congestion of the blood vessels; pons showed very slight congestion; medulla bore no signs of pressure; upper half of cerebellum showed uniform pinking.

Histologically, the pia-arachnoid over the right island of Reil showed miliary tubercles; the lepto-meninges in the other inflamed areas were infiltrated with lymphocytes, few plasma cells, polymorphs, and macrophage cells; the stroma was oedematous. The underlying brain tissue showed mild peri-vascular lymphocytic infiltration of blood vessels, and congestion of deeper one.

The other organs including supra-renals, gall-bladder, kidneys, testes, urinary bladder and the prostate were normal both to naked eye and microscopically.

The middle ears were also normal.

*Discussion.*—The case is an instance of combination of two rather rare processes, miliary tuberculosis of serous membranes without tuberculosis of the invested organs, and a primary brain abscess.

Apart from the miliary tuberculosis in the right island of Reil, the lepto-meningitis was due to the brain abscess; the post-mortem findings were not those of a tuberculous meningitis, but of a septic one. It is considered that two distinctly separate processes were at work, firstly, a miliary tuberculosis of the meninges along with miliary tuberculosis of pleuræ and peritoneum, and secondly, a primary brain abscess ending in fatal lepto-meningitis which is a common mode of termination in cases of brain abscess.

Miliary tuberculosis of the peritoneum is generally due to a blood-borne infection either from the Fallopian tubes, the ovaries, or the mesentine lymph nodes, and even from a distant focus such as the lungs. In this case the spread was probably from the focus in the hilar glands.

Miliary tuberculosis of the pleura has been noticed only rarely without concomitant tuberculosis of the lungs. But a search of several standard books on pathology failed to reveal a combination of miliary tuberculosis as seen in the present case.

The second important feature of the case, the brain abscess, is not so easy to understand. Primary brain abscess is very rare, and yet in this case the abscess had every appearance of being primary. The isolation of the proteus bacillus from two apparently unconnected places suggests a hæmatogenous origin. It is considered that a primary brain abscess merely happened to develop during convalescence from tuberculous pleurisy.

Speculation as to the sequence of events in this case is tempting, but it is felt that the combination of a primary brain abscess with miliary tuberculosis of serous membranes without tuberculosis of the invested organs, is a sufficiently rare phenomenon to warrant recording the case.

Thanks are due to Colonel J. Chandra, O.B.E., I.M.S., Officer Commanding an Indian General Hospital in the M.E., for permission to publish the case; to Captain A. D. Morgan, R.A.M.C., of Central Pathological Laboratory, M.E.F., for help in the histological examination of the tissues; and to Mr. A. C. Lahiri for help in preparation of the article.

## INTRAVENOUS TRANSFUSIONS IN CHOLERA AND OTHER CONDITIONS

### A NOTE ON TECHNIQUE

(The following note written by the editor is based on information provided by Dr. B. C. Chatterjee of the Campbell Hospital, Calcutta, and Dr. B. M. Paul, School of Tropical Medicine, Calcutta.)

WHEN patients are very collapsed and large amounts of fluid have to be given intravenously, it is often difficult or impossible to get a hypodermic needle into a vein, and it is usually best to dissect out a vein at once. The veins of the arm are usually chosen but leg veins may also be used. Even when a vein is dissected out and incised, it is very easy to get the nozzle of the transfusion apparatus in between the coats of the vein instead of in the lumen.

In the cholera wards of the Campbell Hospital, Calcutta, the method here described has long been used, and it appears to be worth publication.

The vein is exposed and two ligatures are placed *in situ* as shown in figures 1 and 2, but only the lower ligature is tied. A surgical needle curved on the flat is then used for transfixing the vein from side to side as shown in figure 3, care being taken that the needle goes



through the centre and the lumen of the vein. The vein is then incised by cutting down on this needle with a sharp scalpel, the cut being made transversely across the vein (see figure 4). The needle serves the very useful purpose of preventing the incision going too deep, and of ensuring that the lumen of the vein is adequately opened.

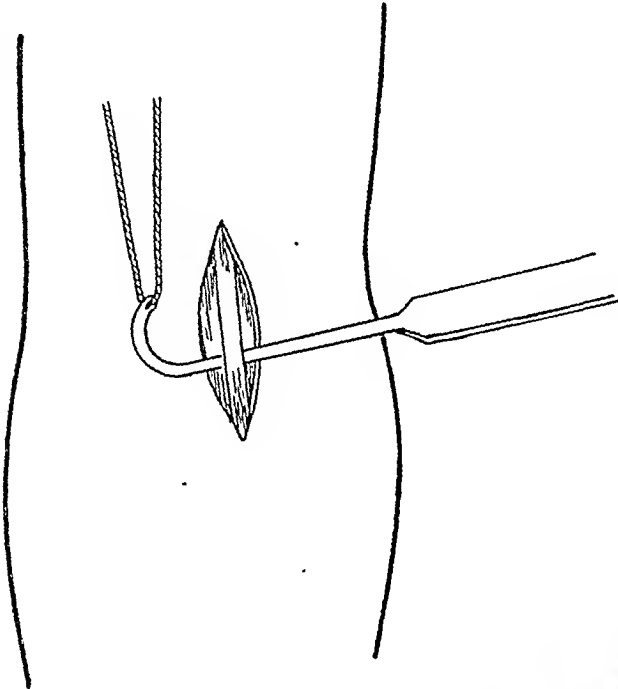


Fig. 1.—Vein exposed and ligatures being placed in position.

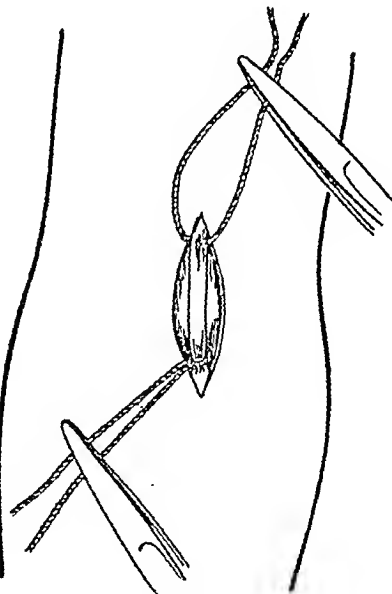


Fig. 2.—The distal ligature tied.

The needle is then removed and is held near the sharp end with a forceps, and the eye end of the needle is passed upwards through the incision into the lumen of the vein (see figure 5). The needle is raised so that the incision in the vein is stretched and there is room underneath

the needle for the insertion of the nozzle of the transfusion apparatus, the needle thus acting as

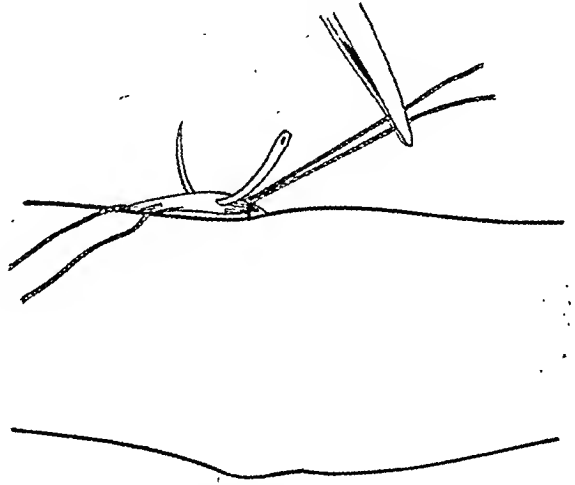


Fig. 3.—Side view showing the vein transfixated with a needle curved on the flat.

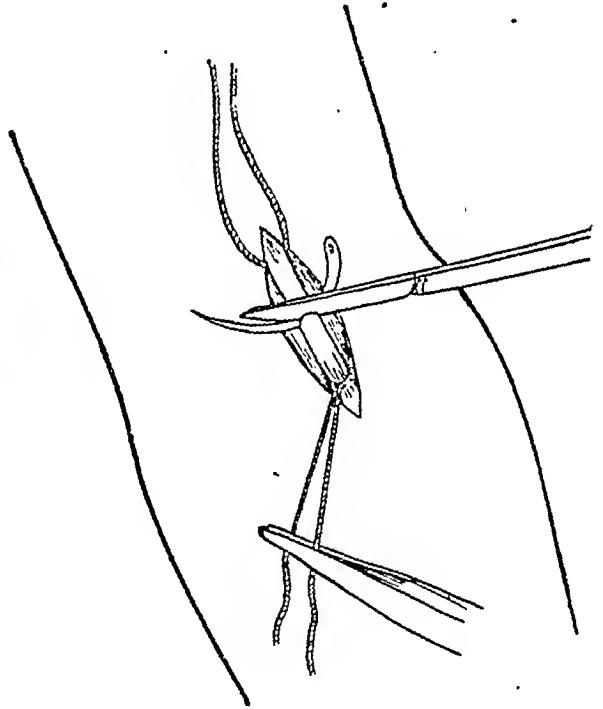


Fig. 4.—The incision of the vein, the cut being carried down to the needle.

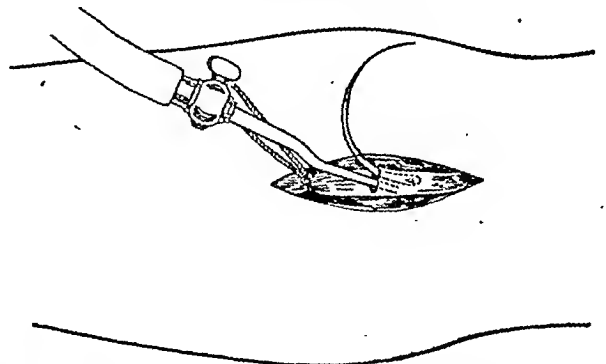


Fig. 5.—The eye end of the needle being used as a director for the insertion of the cannula.

a director. The nozzle is then inserted under the needle and the needle is withdrawn, the ligature being tied lightly round the nozzle to hold it in place.

This method is very rapid, simple and effective, but does not seem to have been published.

## THE VALUE OF D.E.C. MEDIUM IN THE ISOLATION OF INTESTINAL PATHOGENS

By D. W. SOMAN

(From the Haffkine Institute, Bombay)

THE problem of routine isolation of the three principal intestinal pathogens, namely dysentery, enteric and cholera organisms, from faecal specimens is one of vital importance from a clinical and public health standpoint. An efficient selective medium or a combination of such media is essential for the successful isolation of a causative organism. Many types of media have been devised to facilitate this, but few, if any, have proved to be entirely satisfactory for all of them. Recent comparative studies of the different selective media have shown that the time-honoured media such as MacConkey's medium or litmus-lactose agar medium or Endo's medium are far from satisfactory for the primary isolation of pathogens from faeces. The introduction of desoxycholate-citrate agar by Leifson (1935) for the isolation of dysentery organisms marked a great advance over the routine non-selective media used so far. Paulson (1937), Irons *et al.* (1939), Hynes (1942) and Fairbrother (1943) confirmed the superiority of Leifson's medium. Coleman (1940), however, drew attention to the fact that this medium was inhibitory to some strains of *Bacterium shiga*, and therefore it was not reliable for primary isolation of all types of dysentery bacilli. Leifson's medium was subsequently modified by the Difco Laboratories, and their product was called Bacto SS agar; with this medium Mayfield and Gober (1941), Pot (1942), and Rose and Kolodny (1942) reported good results in isolating salmonella and common dysentery organisms, but the results were not as satisfactory in the isolation of *Bacterium shiga*. Panja and Ghosh (1943), while unable to get sodium desoxycholate and some of the bacto-labelled constituents of SS agar, tried to modify Bacto SS agar further; and, by repeated trials, they devised a medium which could isolate not only all types of dysentery bacilli and enteric organisms but also vibrios. On account of the ease with which they could isolate the dysentery, enteric and cholera organisms from samples of faeces, they labelled their modified medium the D.E.C. medium. The consistently poor results obtained by the use of MacConkey's agar and litmus-lactose agar as the media for routine use for faecal cultures in this laboratory led the author to try this new medium. The object of this communication, therefore, is to

verify the claims made by Panja and Ghosh as to the selectivity of their medium over the routine media for the isolation of cholera, enteric and dysentery organisms with special reference to *Bacterium shiga*.

### Material and methods

The general prevalence of intestinal infections during the monsoon, and a small but sharp outbreak of cholera, during the latter part of that season in the city of Bombay and its suburbs, presented an opportunity for comparing the merits of the new D.E.C. medium for the isolation of dysentery, enteric and cholera organisms. The basis of comparison was direct plating on MacConkey agar, litmus-lactose-bile-salt agar and the D.E.C. agar. One hundred and ninety-six faecal specimens were examined, the majority of them being from hospital patients. As this laboratory was situated quite a long distance from various hospitals, the samples of faeces sent could obviously not be fresh. In fact they were definitely more than four hours old. Such samples, when received at the laboratory, were dealt with as quickly as possible. MacConkey agar tubes were kept ready in stock, and the plates were poured when required. Similarly litmus-lactose agar plates and D.E.C. agar plates were also kept ready. D.E.C. agar was prepared according to the formula devised by Panja and Ghosh. Particular care was taken to see that the medium used was not more than a week old, as, according to those authors, the medium deteriorated and became unsuitable for use after that period. Samples of faeces when semi-solid were emulsified with an approximately equal quantity of saline, and, after the heavy particles had deposited, each of the following media was inoculated: MacConkey agar, litmus-lactose agar and the D.E.C. agar. A large inoculum was placed on the D.E.C. plate and streaked freely over the surface. A much smaller inoculum was used for the other plates. In culture samples that were received from acute bacillary dysentery and acute cholera cases, the flakes of mucus, washed in a little saline, were selected for inoculation, rather than the faecal portion. No enrichment media were tried except in the case of cholera stools, which were seeded into alkaline peptone water tubes. For a comparative study of the three media, these results were not considered; direct plating was the only method adopted. Where the enteric group of organisms, especially typhoid, was suspected, a Wilson and Blair's bismuth-sulphite agar plate, freshly poured, was used in addition to the above-mentioned three media. In that case, a large inoculum was heavily seeded over the entire surface, and the plate was incubated at 37°C. for 48 hours. All other plates were incubated at 37°C. for 24 hours only. After overnight incubation, suspicious colonies were fished out to agar slants, were studied as to their microscopical and biochemical characters, and

finally identified by means of slide-agglutination tests with high titre sera.

### Results

A total of 196 stool specimens were examined by the method described above. Eighty-five specimens were received from cases of acute bacillary dysentery, cholera and typhoid, out of which 50 samples proved to be positive for one or other of the pathogenic organisms. The remaining samples were received either from convalescents or contacts, or suspected carriers. Altogether 65 out of 196 specimens were found to be positive on one or more of the four media, as is shown in table I.

an isolation rate of 97 per cent from stool examinations from the 2nd to the 4th day, and in 83 per cent from the 5th to the 7th day of disease. Finlayson (1943) showed that the isolation rate was 86 per cent when stools were cultured on MacConkey agar from the 3rd to the 7th day of disease. After the initial diarrhoea had subsided, the pathogenic bacteria were excreted only intermittently and in small numbers; the value of a selective medium became even more apparent. A reference to tables I and II regarding the isolation of *B. typhosus* from stools would make the point clear. A comparison of cultures on the three media showed clearly that D.E.C. agar was the most

TABLE I  
Total examination

Nature of disease	Total number examined	Total positive	STAGE OF DISEASE			
			Acute		Convalescent or carriers	
			Total examined	Total positive	Total examined	Total positive
Bacillary dysentery ..	88	18	27	14	61	4
Enteric fever ..	37	12	2	1	35	11
Cholera ..	71	35	56	35	15	0
TOTAL ..	196	65	85	50	111	15

Failure or success of isolation of a pathogen depends on a number of different factors such as the freshness of the sample and the preserving fluid in which it is sent, the stage of disease at which it is being examined, and the selectivity of the medium used for isolation. The samples received by this laboratory from various hospitals, situated at a considerable distance, could obviously not be fresh, and were not sent in any kind of preserving fluid. In the absence of such ideal conditions, 50 positive isolations could be obtained out of 85 samples from cases in the early stage of the disease, giving a rate of only 58 per cent. This would have been still lower had it not been for the inclusion of the new medium, a fact which would be easily apparent by the study of table II.

### Discussion

The results shown in tables I and II clearly indicate that a large proportion of positive specimens would have been missed if the routine non-selective media alone had been depended upon. Moreover, most of the isolations on litmus-lactose agar and MacConkey agar were obtained from patients early in the course of the disease, when many of the pathogens were being constantly excreted in the stools. Anderson, Cruickshank and Walker (1941) reported

TABLE II  
Results with different media

Causative organism	Total positive	D.E.C. positive	LLA positive	Mac. positive	B.S.A. positive
<i>B. dysentery</i> group	18	16	5	3	..
<i>V. cholera</i> ..	35	33	19	28	..
<i>B. paratyphosus</i> A.	1	1	1	1	..
<i>B. typhosus</i> ..	11	10	0	0	8
Total ..	65	60	25	32	..
PERCENTAGE POSITIVE	..	92	38.4	49.2	..

LLA = Litmus-lactose agar; Mac. = MacConkey's agar; B.S.A. = Bismuth sulphite agar.

selective of the group, and supported the growth of all the three most important intestinal pathogens. D.E.C. agar gave 92 per cent positive results, whereas the other two gave 38.4

per cent and 49.2 per cent respectively. It might be interesting to observe that D.E.C. agar failed to isolate the causative organisms in five cases in which they could be isolated on the routine media. It was later revealed that in two cases of *B. flexner*, the D.E.C. agar plates used were more than ten days old. In the remaining three cases, the medium failed in the isolation of *V. cholera* twice and *B. typhosus* once. The cause of these failures remained unascertained.

The number of faecal samples examined for the diagnosis of dysentery, and the total number of positive isolations on the three different media have been given in tables I and II. Dysentery organisms could be isolated on D.E.C. medium 16 out of 18 times. The other two media gave very poor results. All the types of dysentery bacilli could be isolated, but *B. shiga* has been reported to be rather fastidious in regard to its growth requirements by a number of workers using different selective media. In view of this fact, it would be still more interesting to tabulate the number of positive isolations according to the types of dysentery bacilli and the media from which they were isolated.

TABLE III  
Different organisms and different media

Organism	Total	D.E.C.	LLA	Mac.
<i>B. flexner</i> ..	12	10	3	2
<i>B. shiga</i> ..	1	1	0	0
<i>B. sonne</i> ..	4	4	1	0
<i>B. schmitz</i> ..	1	1	1	1
<b>TOTAL</b> ..	<b>18</b>	<b>16</b>	<b>5</b>	<b>3</b>

A reference to the above table showed that *B. flexner* was the most prevalent type causing dysentery infection in Bombay at the time, and that *B. shiga*, *B. sonne* and *B. schmitz* played only a minor part. *B. shiga* was isolated only once out of 18 positive cultures, and that only on the D.E.C. medium. On the result of such a single isolation, it would be unwise to suggest that D.E.C. medium was equally reliable for primary isolation in shiga infections. Panja and Ghosh, in artificial mixtures of normal stools and *B. shiga* suspensions, showed that their medium did support the growth of this organism, although the colonies obtained on their medium were relatively small. Moreover, they stated that out of 22 positive isolations, they could isolate *B. shiga* along with other dysentery bacilli from dysentery stools; but they have not stated the number they had isolated. Therefore, many more comparative observations would be necessary before D.E.C. medium is accepted as equal or even superior to other selective media in this respect. All dysentery organisms, including *B. sonne*, appeared on D.E.C. medium as translucent colourless

colonies. The colonies of *B. shiga* were, however, very small. The new medium did not affect the agglutinability of the dysentery organisms when examined by the slide-agglutination test.

The number of samples examined for the diagnosis of enteric or typhoid was 37, out of which 35 came from convalescent patients prior to their discharge from hospitals. The gross failure of the non-selective media and the corresponding success in isolation on the selective media strongly suggested that the organisms excreted in faeces were in small numbers, and further demonstrated the selectivity of the two media. A comparison between these two selective media indicated that D.E.C. medium compared very favourably with the other, although, the number of specimens being relatively small, no statistical evaluation of the media could be made. Actually, where D.E.C. medium failed once to isolate *B. typhosus* which could be isolated on the other, the B.S.A. medium failed thrice. The failure of B.S.A. medium might perhaps be attributed to an observation by Tabet (1938), that some strains of *B. typhosus*, being very sensitive to this selective medium, failed to grow. Whether it would hold good in the case of D.E.C. medium is not known. The use of D.E.C. medium would be more advantageous than the use of B.S.A., because the medium did not interfere with the agglutinability of the colonies, these being picked up and identified in 24 hours; the medium kept well and serviceable at least for a week. Colonies growing on a B.S.A. medium could not be used for the slide-agglutination test, and they developed their typical black metallic sheen in 48 hours; the completed medium deteriorated rapidly and even the freshly prepared medium was known to inhibit growth of some strains of *B. typhosus*.

The number of samples examined for the diagnosis of cholera was 71, out of which 56 samples presented a typical rice-water appearance with or without bile staining. *V. cholera* could be isolated from 35 samples. Again D.E.C. medium proved the best of the lot. While recovery of *V. cholera* from fresh specimens of stools is comparatively easy, satisfactory examination of specimens obtained at a distance from the laboratory presents great difficulties, as *V. cholera* dies off rapidly in stored specimens of stools, and is easily overgrown by other intestinal organisms. The method of peptone-water enrichment was found to be less satisfactory than direct plating on D.E.C. agar. No other selective media, such as the Aronson's medium or Read's modified Wilson and Blair medium, was tried. It might be of interest to note that even on standard agar tubes, *V. cholera* could be isolated 24 times from 35 samples; this suggested that in the very early and acute stage of this disease, the stool being almost a culture of *V. cholera*, the kind of medium used did not matter so long it was not actually inhibitory. All strains isolated

were agglutinable with the cholera O serum group I, non-hæmolytic, and were found belonging to Ogawa type. Only 15 samples of stools were received from contacts of cholera cases, and none of them showed any positive result. NAG vibrios were isolated three or four times only.

### Conclusions

D.E.C. medium was easy to prepare and when ready it was clear and translucent. The dysentery, enteric and cholera organisms grew well on this medium as colourless colonies in 24 hours. *Bacterium coli* and other intestinal saprophytic organisms were largely suppressed. Coliform organisms when present appeared as pink colonies. Contamination of plates with fungi and sporeformers was rare. The new medium was found to be definitely superior to the routine non-selective media, and its superiority was more marked in convalescence. No one single medium being found suitable for the primary isolation of all intestinal pathogens, a strong plea is made to adopt the new medium for routine use in every bacteriological laboratory. The use of such a medium should increase the efficiency of methods for the bacteriological examination of faeces, a matter of importance to public health, from the standpoint not only of diagnosing these three infective conditions, but also of recognizing carriers due to them.

[It might be pointed out that 22 more positive isolations have been obtained since D.E.C. medium was accepted as the medium of choice for routine use in this laboratory. However they could not be incorporated into the previous results as they were not comparative. *B. dys. flexner* 10; *B. dys. shiga* 4; *B. dys. sonne* 5; *B. typhosus* 3; total 22.]

### Summary

(1) A comparison was made of the value of three media, namely MacConkey agar, litmus-lactose-bile-salt agar and D.E.C. medium devised by Panja and Ghosh, for the primary isolation of dysentery, enteric and cholera organisms from faeces. A total of 196 samples was examined out of which 65 samples gave positive isolations. D.E.C. medium facilitated the growth of the three pathogens in 92 per cent of positive isolations. The results of the other two media were extremely poor.

(2) If one selective and solid medium were to be chosen for isolation of all three intestinal pathogens, D.E.C. medium would seem to be the best choice.

(3) In a small series of typhoid cases, D.E.C. medium compared very favourably with the Wilson and Blair's bismuth-sulphite agar medium in the isolation of *B. typhosus* from faeces.

(4) The new medium should prove to be a most valuable addition to the existing selective and non-selective media, and should be adopted for routine use in every bacteriological laboratory.

### Acknowledgments

I have to thank Mr. Nail and Mr. R. C. Vaidya, B.Sc., for their technical assistance.

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## A Mirror of Hospital Practice

### ANGIONEUROTIC OEDEMA

#### PRODUCED BY SULPHATHIAZOLE

By J. N. BERRY, M.D.

Lahore

A HINDU male, aged 25, was given sulphathiazole for nasal sinusitis after a common cold; first dose (4 tablets) given at night. Late at night he woke up with itehiness of the scalp and in the morning he had puffiness and oedema of the face and scalp (giving a wrinkled baggy appearance to the face). It was soon relieved by an injection of adrenalin. No more of the sulpha-drug was taken.

A year later the same treatment was followed by the same result.

The patient has a family history of asthma and has himself suffered occasionally from such attacks, lasting for a variable period. The second time, he was actually in such an attack. No other drug was being administered on either of these occasions. He has not suffered from urticaria or angioneurotic oedema at any other in his life. No such symptoms were produced after sulphanilamide therapy on another occasion.

### Comments

It is evidently a case of angioneurotic oedema following sulphathiazole administration. It is a very uncommon manifestation of allergy to sulpha-drugs, and, as far as I could find, it has not been recorded so far. As the patient has shown no allergic manifestation to sulphanilamide, the hypersensitive reaction to sulphathiazole must be due to the thiazole radicle, and it is unlikely that he will be susceptible to the other drugs of the series which do not contain the thiazole radicle. Recent work of Park (1944) supports this presumption.

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- PARK, R. G. (1944). .. *Brit. Med. J.*, i, 781.

# HIGHLY POTENT WHOLE LIVER EXTRACT

HG RBC  
% count

100 5

90 4.5

80 4

70 3.5

60 3

50 2.5

40 2

30 1.5



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# Indian Medical Gazette

OCTOBER

## BLACKWATER FEVER AND METHÆMALBUMIN

BLACKWATER FEVER remains one of the unsolved problems of tropical medicine. While its relationship to malaria is generally recognized, the exact nature of this relationship is unexplained. Some consider that a special strain of the parasite is responsible, but there is considerable evidence against this; the inoculation of healthy persons with the blood of blackwater fever cases nearly always produces malaria but not blackwater fever; there appears therefore to be some factor in the patient himself apart from the parasite. The relation of blackwater fever to quinine administration has long been recognized, but the nature of this relationship also is obscure. The fundamental pathological processes in blackwater fever are still unknown, but in recent years several papers have been published which throw light upon this subject. This recent work on blackwater fever done in other countries does not appear to have attracted much attention in India, and therefore we attempt here to summarize some of this work. [The information given here is abstracted from the *British Encyclopædia of Medical Practice, Cumulative Supplement*, 1943, p. 53 *et seq.* The credit for the discovery of the new pigment methæmalbumin apparently is due to Fairley, whose masterly study of the blood pigments (*Quarterly Journal of Medicine*, 1941, vol. X, pp. 95, 115) should be studied by all interested in the subject.]

The studies of H. Foy, A. Kondi and A. Moumjidis showed, as already stated, that the injection of blackwater fever blood into a normal person produced an attack of malaria with *P. falciparum* but not blackwater fever. The transfusion of normal blood to blackwater fever patients was followed by rapid hæmolysis of the transfused cells, which is evidence that the change is not in the cells of the blackwater fever patient.

A study of the pigments present in the blood and urine of blackwater fever cases has given interesting results. Long ago Yorke and later others recorded oxyhæmoglobin and methæmoglobin in the plasma in blackwater fever. It appears, however, that the pigment present is one previously unrecognized. It was first called pseudo-methæmoglobin, and it is now called methæmalbumin. It is constantly demonstrated in the plasma of blackwater fever cases, whereas methæmoglobin does not occur in the plasma. (The presence of methæmoglobin in

the urine of blackwater fever cases is due to the alteration in the hæmoglobin during excretion.) The new pigment is identified by spectroscopic methods, or by a combination of these and chemical methods. It is produced by the action of plasma upon hæmoglobin liberated from the red cells, and its presence therefore indicates intravascular hæmolysis. The change can be produced *in vitro*; actually this is the body's normal method of eliminating free circulating hæmoglobin. When methæmoglobin is produced in the blood by the action of some drugs, it is present in red cells and not in plasma.

Fairley has made a detailed study of the pigments occurring normally in the body and in pathological conditions, and has particularly made studies of the new pigment methæmalbumin. This new pigment is found in the blood plasma in blackwater fever, and also in nocturnal and paroxysmal hæmoglobinuria and incompatible blood transfusion. It is also found in some forms of hæmolytic anæmia. It has been detected in pancreatic cyst fluid also. It is never found in the urine, since the molecule is too large to pass through the kidney. The new pigment is considered to be a combination of hæmatin with serum albumin, analogous to but different from methæmoglobin which is a combination of hæmatin with globin.

This new pigment is not merely of theoretical importance but of practical value in the diagnosis of blackwater fever. In the tropics, any case of hæmoglobinuria tends to be regarded as blackwater fever, especially in areas where blackwater fever is known to occur. Hæmoglobinuria however may be produced by a large number of causes, which include the action of drugs including the sulphonamides, plasmochin, quinine, and atabrin. Paroxysmal hæmoglobinuria also is not of uncommon occurrence. Another form of hæmoglobinuria is nocturnal hæmoglobinuria or the Marchiafava-Micheli syndrome. The study of the pigment present in the blood is of considerable value in sorting out hæmoglobinurias into their different types. If the hæmoglobinuria is the result of intravascular hæmolysis, as seen in blackwater fever, nocturnal and paroxysmal hæmoglobinuria and incompatible blood transfusion and some anæmias, then the pigment methæmalbumin should be found in the blood plasma. If however the hæmoglobinuria is the result of the administration of drugs, then no methæmalbumin should be found in the plasma, but methæmoglobin will be found in the cells.

Part of the difficulty in the study of blackwater fever, its ætiology and its treatment, commonly lies in the fact that some cases regarded as blackwater fever are not true blackwater fever, and the study of the blood pigments, by making accurate differentiation possible, should be a great help. The presence of methæmalbumin in the blood plasma however does not prove that the case is one of blackwater fever. Paroxysmal hæmoglobinuria can

be diagnosed by the demonstration of the occurrence of agglutinins in the blood, and by the occurrence of 'autohaemagglutination' at temperatures below that of the body. Nocturnal haemoglobinuria does however present a problem; the haemoglobinuria is detected in the early morning and does not occur in the day, whereas in blackwater fever the haemoglobinuria is much more constant.

It appears to us highly desirable that, in future studies of blackwater fever in India, this new knowledge should be made full use of, and that with more accurate diagnosis and the exclusion of those cases that are not true blackwater fever, some of the problems of this interesting disease, blackwater fever, may be more easily solved.

One difficulty lies however in the fact that blackwater fever commonly occurs far away from centres where spectroscopic examination of the blood for pigments can be carried out. The editor is making arrangements for the examination for methaemalbumin to be carried out in the School of Tropical Medicine, Calcutta, and if any doctors have cases of haemoglobinuria in which they would like to have this test done, an ampoule of sterile oxalated blood or plasma should be sent to him there with case notes, and the examination will be done and the report sent.

J. L.

### COMPLEMENT FIXATION IN KALA-AZAR WITH THE WKK ANTIGEN

IN our present issue we publish two articles in which the value of a complement-fixation test

in early diagnosis of kala-azar is stressed. The antigen used is that of Witebsky, Klingenstein and Kuhn prepared from the tubercle bacillus, and originally intended for complement-fixation tests in tuberculosis. In tuberculosis, however, the results are very poor. Work in South America, however, revealed other possible uses of the antigen. Bier (1936) studying the use of antigen in leprosy, included some cases of leishmaniasis as controls, and reported 75 per cent positive results in leishmaniasis. In 1938, Lowe and Greval in India confirmed this, recording positive results in all 17 cases of kala-azar tested. Since then others, mainly Sen Gupta, have developed this test, and the technique has been improved. It appears that this test will become a routine test in kala-azar where practicable, since it is much superior to the older aldehyde and antimony tests.

So far no person's name has yet been attached to this test, and it would appear better not to attach a person's name. It is at present known as the complement-fixation test with WKK antigen. This antigen was marketed under this name before the war and will probably reappear on the market. It is at present being prepared and used in the School of Tropical Medicine. The test is being applied with considerable success in the diagnosis of cases of early kala-azar seen in the army. Cases in the civil population tend to come later, but here also its use has greatly facilitated early diagnosis in a number of cases.

J. L.

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## Special Articles

### TRANSMISSION OF KALA-AZAR IN INDIA

#### THE CASE AGAINST THE SANDFLY

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EXPERIMENTS and observations made by workers in India on *P. argentipes* in its relation to kala-azar present four phases. In the first, attention is directed to the study of the sandfly in nature and under laboratory conditions simulating as closely as possible those found in nature, e.g. in the earlier work of Christophers and in the stress laid on field work by Mackie and others. Failure to incriminate the sandfly followed these efforts. In the second phase, a

departure from these sound principles is evident, and laboratory experiments predominate under conditions which become more and more unlike those found in nature, e.g. segregation of the sexes as a means of prolonging the life of the female. In this phase, workers seem to have convinced themselves that the sandfly must be the natural vector of the disease, and all their efforts are directed towards devising experimental conditions which would produce the desired result. Their efforts appeared to be crowned with success when Knowles announced infection by flagellate forms of *L. donovani* extending into the buccal cavity of *P. argentipes*, and it was considered that the case for the sandfly had been proved except for demonstration of the actual transmission of the disease to human volunteers. These transmission experiments failed. Then follow years of disappointment; the sandfly retires into the background, epidemiological evidence which does not support

the sandfly theory accumulates, and excellent work is produced to show that kala-azar can be transmitted by contact and by ingestion of the parasites. In the fourth phase, the sandfly is again attacked in the laboratory, though hardly in the field, by special methods and techniques under conditions of a highly artificial nature largely developed by Smith, and, finally, Swaminath, Shortt and Anderson (1942) report the successful transmission of kala-azar by the bites of experimentally infected *P. argentipes* in every one of seven volunteers bitten.

This is now regarded as the final proof that this sandfly transmits kala-azar in nature—the proof eagerly awaited by the medical world after more than 20 years of unremitting research. It might thus seem an impertinence to re-open the question and to suggest that *P. argentipes* may not be the natural vector of kala-azar. Nevertheless, a careful study of the published papers of the workers, especially in India, who have devoted their time and energies to the study of this disease—and the elusive *Phlebotomus*—have convinced us that their work supplies abundant evidence that *P. argentipes* is not the natural vector, and indeed, that the life history of *P. argentipes*, as observed under natural conditions, precludes it from being the natural vector of any human disease whatsoever. What has been proved is that, under certain highly artificial conditions, this insect may serve as a culture medium in which the parasite multiplies, and may be induced experimentally to transmit the disease. This appears to us to be a far cry from proving that it is the natural vector. Successful transmission of the disease has been achieved by a special technique of breeding and feeding *P. argentipes* in the laboratory by means of which the duration of life of the flies has been prolonged to ten days or longer, thus permitting the flagellate forms to develop fully: the flies have been induced to take more than one blood meal, and they have been 'blocked' as the result of an artificial diet of raisins.

We believe that none of these phenomena occurs in nature, and that without them *P. argentipes* cannot be the natural vector of kala-azar.

We base our conclusions entirely on a critical study of papers published in medical journals in India and elsewhere. The arguments are detailed under the following heads:—

- (1) Bionomics of *P. argentipes*.
- (2) Epidemiological factors.

#### BIONOMICS OF *P. argentipes*

##### (a) Duration of life and feeding habits in nature and in the laboratory

Smith *et al.* (1936) released marked *argentipes* on the day they emerged from their pupal cases in places where these sandflies were naturally breeding. In his first experiment, where marking was done by the dusting of fluorescein or by the removal of one middle leg, out of 667 flies released recoveries were as follows:—

Day after release ..	1	2	3	4	5	6	7	15th
Flies recovered ..	..	..	..	1	2	..	4	2

Identification by means of a missing leg in so delicate an insect is obviously open to fallacy, and that this struck the author is shown by his subsequent experiments in which this method of identification was abandoned in favour of wing puncture. In these subsequent experiments 3,271 flies were marked by fluorescein or by wing puncture. Re-captures were as follows:—

Day after release ..	1	2	3	4	5	6	7	onwards
Flies recovered ..	79	18	9	7	2	3	nil.	

Again, similarly marked flies were released and search made for them after some days—of 428 flies looked for on the 9th, 16th, and 19th days, not one fly was re-captured. It should be noted that search to re-capture the flies was made 'by the same three men especially trained in the collection of these midges for periods varying from four to ten years', and the author, who gave well-reasoned views for assuming that the flies would not migrate, himself observes, 'our previous assumption that the flies did not migrate to any extent was correct'.

If then (after a reliable method of identification had been introduced), not a single fly out of 3,271 + 428 could be re-captured by these experts after the sixth day and the flies did not migrate, it seems fair to conclude that *P. argentipes* in natural surroundings does not normally, live longer than six days.

This is in large measure confirmed by the earlier work of Christophers which showed that female sandflies, bred in the laboratory or caught in nature and kept under the most natural and favourable conditions possible, invariably died immediately after ovipositing (Christophers *et al.*, 1926, 1926a).

Again, it has been shown by Shortt that males and females hatch out in equal numbers and that the males live for only one or two days, dying soon after copulation. If the females lived for ten days in nature, as they can be induced to do under certain laboratory conditions, one would expect catches of flies to show a distinct preponderance of females. Especially should this be the case if the females leave their crannies to feed on more than one occasion, as they must do if they are to be vectors of kala-azar. Such a preponderance has never been observed, although the reverse (i.e. an excess of males) has not been an unusual finding.

Attempts have been made to prolong the life of the flies, and Shortt *et al.* (1926a) succeeded in doing this by segregation of the sexes, thus preventing fertilization and oviposition. It is obvious, however, that this highly unnatural procedure could never obtain in nature.

Some time later, Shortt *et al.* (1926a) developed a technique depending on rigid control of conditions of temperature. They succeeded in keeping female flies alive for ten days or longer, and induced them to take more than one blood meal. By this means, flagellate infections extending to the buccal cavity were obtained.

It was claimed that the conditions under which the laboratory flies were kept were comparable to those obtaining in Assam, during the monsoon months, and therefore simulated natural conditions.

This does not appear to be so, for while the experimental flies required a uniform temperature of 28°C., and a variation of more than 2°C. proved fatal, the official records show that the average temperatures recorded at Dibrugarh, Sibsagar, Tezpur, Gauhati, Dhubri, Silchar and Srimangal in Assam were fairly uniformly 30°C. throughout the months of May to August, and that the daily variations were always greater than 5°C. at any of these places—a variation too great for laboratory-kept flies to withstand.

Again the Indian Kala-azar Commission found that the range of temperature for the successful feeding of flies was also limited. The limits were wide—from 17°C. to 28°C.—but the optimum temperature for feeding was 24°C., and they state 'when the temperature reaches the upper and lower extremities, it is found not only that a smaller percentage of flies will feed but that those that do so are only partially fed. These flies are of little subsequent use, and we have found that they almost invariably die on the third day'. Accordingly the flies were kept at a uniform temperature of 28°C. except when they were fed, when they and the experimental animal were placed for one hour in an incubator at 24°C. This is unnatural, for sandflies will normally feed at dusk and the night temperature will fall consistently between dusk and dawn. Even if it be maintained that the room temperature may differ from that of cracks and crannies to which sandflies may return after feeding, there yet remains a difficulty. Just during the months of May to August inclusive, when laboratory conditions most closely simulated natural conditions in Assam, it was found that 'whatever means be taken to encourage it, satisfactory feeding has not yet been found possible' (Shortt *et al.*, 1926a). The Commission offers no explanation for this remarkable observation.

It cannot be taken for granted that natural conditions are necessarily better than artificial conditions. All life is a struggle to adapt itself to adverse conditions, and if all that is adverse is removed, there is no reason why life should not be considerably prolonged—for man, mosquito, sandfly, germ or virus. That nature does not provide a suitable temperature in Assam for prolonging the life of the sandfly or for inducing it to re-feed seems to be borne out by this finding of the Commission as well as by the actual records of the Meteorological Department. Nor can it be maintained that such optimum temperatures are to be found in other places, e.g. Pusa and Sanawar, where the coincident presence of *argentipes* and kala-azar is said to be evidence of a causal relationship between the two.

Further evidence that these conditions are unnatural is found in the statement of Shortt *et al.* (1932):

'Copulation among flies occurs either before or just after the first feed. . . . If a large number of flies are bred out in the laboratory and the mixed sexes are released in a muslin cage, within the first 24 hours practically all the females have become fertilized. . . .

On a number of occasions we have released male flies into a muslin cage containing flies that had had two, three or four feeds, yet on no occasion has any pairing been observed. These facts would point to the conclusion that fertilization occurs but once in the life of the female and that it takes place usually before the first meal. . . . The males never live long after copulation even when they are provided with food material in the form of solutions of glucose and it seems that in performing the act of fertilizing one female they have paid their full debt to nature. Another point that seems to point to the same conclusion is that from a given number of eggs equal number of males and females hatch out. . . . Our experience with such batches was that, as a rule, the female was the first to hatch and this seems to be a provision against any possible bar to fertilization of the females due to the short life of the male.

Again it should be noted that in the observations of Christophers *et al.* (1926) there is not a single instance of a caught gravid fly (*i.e.* one which had fed under natural conditions) ever taking a second meal when given an opportunity to do so.

It would appear that under natural conditions the female as well as the male is short-lived, and if by fertilizing one female the male pays its full debt to nature, it is probable that in ovipositing the female also pays her full debt to nature, as suggested by the work of Christophers *et al.* (1926) quoted above.

It has been repeatedly maintained that *Phlebotomus*, in nature, are solely blood-feeders. Napier and Smith (1926a) state—

'The adult female sucks blood and is a pure blood-feeder.' 'The normal life cycle of this fly appears to include only one meal' (Napier and Smith, 1926). 'Attempts were made to feed adult males on sugar, fruit and plant juices, but they were never observed to take any food. The adult female is exclusively a blood-feeder normally taking only one meal' (Napier and Smith, 1926a).

These statements may, of course, have been the outcome of insufficient knowledge of the feeding habits of these flies at the time they were made. But we must emphasize the fact that no evidence has yet been afforded to disprove that *P. argentipes* are pure blood-feeders in nature, or when given free choice to feed on blood or plant juices.

We believe that the experimental prolongation of life and re-feeding have no biological significance whatever.

#### (b) Flagellate infections in the laboratory

We have shown that, by means of a special and highly artificial technique, Shortt succeeded in producing flagellate infections in *P. argentipes*. At that time it was believed that the problem of the transmission of kala-azar had been solved, and that nothing remained but to demonstrate the actual infection of human volunteers by the bites of such infected sandflies. However, these experiments failed, and it was not until 16 years later that success was obtained after further modifications of Shortt's technique.

If Shortt's technique is artificial, the final technique which has resulted in successful transmission is still more so. Not only is Shortt's



uniform temperature maintained, but a special diet of raisins is introduced. Special attention is also paid to humidity, and by these means *P. argentipes* are rendered infective on the tenth day after the first blood meal. Meticulous care is taken over the quality, preparation and treatment of the raisins. Smith *et al.* (1940), who originally devised this technique, are constrained to admit, 'the conditions seem unnatural and unlikely to yield satisfactory results' though they try to conceal this admission by adding: 'The fact that *P. argentipes* are most prevalent in rural areas where the opportunities of imbibing plant and fruit juices are present practically throughout the year would favour such a possibility . . . . It must, however, be stated that repeated attempts to capture flies from such situations have up to now not yielded any encouraging results'.

Furthermore, Shortt *et al.* (1932) state, 'so far as our experience went, *P. argentipes* always breeds inside or in the immediate neighbourhood of houses or animal sheds. A systematic search of the soil in situations removed from houses and cattle-sheds, but otherwise suitable for breeding purposes, has never yielded any larvæ, and trap nets set in similar situations to catch adults have also yielded no *argentipes*'.

It would appear (though it is not expressly stated) that the successful transmission experiments in human volunteers were carried out with 'blocked' flies, but the phenomenon of 'blocking' is artificially produced, and has never been observed in caught flies—quite unlike the phenomenon in plague fleas—and we consider it highly improbable that such a condition could happen in nature where flies do not feed on raisins and do not live long enough for 'blocking' to occur.

#### (c) *Flagellate infections in nature*

Shortt *et al.* (1932) state—

'By the fifth day the flagellate infection may have reached the pharynx of the fly. By the sixth day the whole pharynx may be involved. By the seventh day the infection may reach the junction of the pharynx and the buccal cavity. By the eighth or ninth day the buccal cavity may show a massive invasion. . . .

These statements refer to flies kept under rigidly maintained artificial conditions, but, in 20 years of unremitting research, not a single *P. argentipes* has ever been recorded with a natural infection of *L. donovani* extending to the pharynx or beyond. Instances of natural infection to a slighter degree in any sandflies, thought to be vectors of kala-azar, are remarkably few, although thousands of flies have been examined. Thus, a naturally infected sandfly has never been recorded from China. In India, Shortt, Barraud and Craighead (1926) found their first naturally positive fly, on the 26th July, 1926, after the Commission had been in operation for close on three years. Four years later, Shortt, Craighead, Smith and Swaminath (1930) reported seven positive flies out of 226

examined, and it is sometimes assumed on the strength of this finding that about 3 per cent of *P. argentipes* in kala-azar areas are naturally infected. That this is not so is proved by the earlier negative findings of the Commission. Moreover, with regard to these seven positive flies, six were from a batch of 69 *P. argentipes* caught in a cattle-shed, not as stated by Wenyon (1932) from kala-azar houses. If however, as is frequently stated, sandflies seldom, if ever, fly from one house to another, and since cattle-sheds are favourite breeding sites for *P. argentipes*, it is unlikely that all of the 69 flies had migrated from kala-azar houses. Thus, assuming the source of infection to be human, these six positive flies would represent an infection rate of considerably more than 10 per cent. With such a high infection rate, the failure to find a fly with a pharynx infection becomes still more inexplicable.

More than ten years later, Smith *et al.* (1941) report 'the number of naturally infected *P. argentipes* found up to date is remarkably small and quite out of proportion to the incidence of the disease in endemic areas'. The authors attempt to explain this by suggesting that 'blocked' flies have been missed since they cannot easily be distinguished from newly hatched unfed females. But not a single 'blocked' fly has ever been found in nature either before or since this observation.

Though we are not concerned with oriental sore in this paper, it is noteworthy that, amongst all the sandflies examined in this connection, there has been only one naturally infected fly in which the infection extended to the pharynx, and even with regard to this fly there is considerable doubt as to the source of infection (Adler and Theodor, 1926).

No argument based on the experimental transmission of oriental sore can be regarded as valid for kala-azar, for, despite the years of research devoted to oriental sore, it has not yet been proved that a sandfly caught in nature can transmit the sore by its bite.

#### (d) *Other biological considerations*

Kala-azar is a disease of the reticulo-endothelial system and of the skin. It cannot be regarded as a disease of the blood stream. Writing in 1926, after flagellation and anterior development in the sandfly was a well-established fact, Christophers (1926) stated 'the fact remains that in kala-azar, there does not appear to be any special provision, as in the cases of malaria, filaria, etc., for the parasites to be taken up by a blood-sucking insect'. In all diseases of the blood stream, where transmission is by a blood-sucking insect (e.g. malaria, filaria, trypanosomiasis), and in other diseases where the blood stream is invaded (e.g. rat-bite fever, septicæmic plague), parasites are found either attacking red cells or living free. In kala-azar, parasites may occasionally be found free in the blood stream, but for the most part



they are within the leucocytes and particularly the large reticulo-endothelial cells where they are phagocytosed or, having ruptured one cell, are about to be phagocytosed. The presence of the parasite in the blood stream then can only be regarded as an accident for the parasite rather than a biological necessity.

Arguing from analogy, protozoologists take for granted the fundamental assumption that an insect vector must be involved in the transmission of kala-azar. No parasite having the life cycle of *L. donovani* is transmitted in any way other than by a biting insect. This is so generally true that it would outweigh any evidence to the contrary were it not for certain unique differences which kala-azar exhibits when compared with insect-borne diseases. That the assumption may be wrong is shown by the following facts:—

(a) In diseases transmitted by an insect vector, infection can be experimentally transmitted only by the bite of the infected insect (or its laboratory equivalent, inoculation). Malaria, trypanosomiasis, yellow fever, relapsing fever, typhus, bubonic plague, all illustrate this. But Shortt *et al.* (1932) have shown that kala-azar may be experimentally transmitted with comparative ease to Chinese hamsters by ingestion and proximity.

(b) In such diseases, the parasite is in the blood stream; in kala-azar it is more probably in the skin.

(c) Flagellates of closely allied diseases (*e.g.* trypanosomiasis) will cause the disease when injected intravenously. Archibald (1914) and Knowles *et al.* (1923) showed that the flagellates of kala-azar were instantly destroyed when so injected.

(d) Nature does occasionally provide exceptions to general rules. Thus, *T. equiperdum*, in contradistinction to other trypanosomes, is normally transmitted by direct contact (coitus), and no intermediate host is necessary.

It is known that a mosquito may be an efficient vector of malaria in one place but not in another. This, however, is very much the exception and not the rule. But if the sandfly is the vector of kala-azar, this exception becomes the rule.

*P. perniciosus* is the suspected vector in Mediterranean areas but not elsewhere where it is found. *P. major* var. *chinesis* is suspected in China [despite Young and Hertig's (1928) findings to the contrary], and in India *P. argentipes* is suspected where kala-azar occurs, but there is no satisfactory explanation for its failure to transmit the disease in places such as Ceylon and Bombay where it is also found. Recently, yet another sandfly, *P. congolensis*, has been suggested as the probable vector in Central Africa (Anderson, 1943).

It is a well-established fact that insects which are not vectors of a disease in nature may be experimentally rendered infective. Thus, in yellow fever, many species of *Aedes*, in addition to *A. aegypti*, and even other genera can be made to transmit the disease experimentally to Rhesus monkeys. And similar findings are

known in connection with *Anopheles* and malaria.

The mere fact that flagellation takes place in the sandfly is not necessarily of biological significance. Similar flagellation takes place in the bed bug, and the 'anterior development' in the sandfly, as we have seen, only takes place when the life of the fly is artificially prolonged. Besides, as Mackie (1922) points out, 'the fact that flagellates of a water scorpion can give rise to leishmania-like infection in mice, a parasite and host that would never come together in nature, induces a complexity to the problem...' The aetiology of kala-azar is indeed so complex that it would appear to be unwise to attach too much importance to any one set of factors. For example, dysenteric symptoms, so common in kala-azar, are in almost all other diseases of distinct biological significance, and where they occur infection is usually by ingestion.

#### EPIDEMIOLOGICAL FACTORS

(1) *Distribution of P. argentipes and kala-azar.*—It is generally assumed that the distribution of kala-azar coincides with that of *P. argentipes* in India. The credit for this observation is due to Sinton who first pointed it out in a private communication to Knowles and Napier in 1922. Sinton (1924) states 'like kala-azar its distribution seems to be bounded north and west by a line joining Delhi and Bombay'. Napier (1926) notes 'it has been repeatedly stated by careful observers that the disease does not occur west of Lucknow', and this is generally accepted as true. It must, however, be admitted that while the distribution of kala-azar is fairly well defined, that of *argentipes* is very imperfectly known. Sinton (1925) states 'as our knowledge of the distribution of the various species of the *Phlebotomus* on the eastern side is still very scanty, it may be found on further investigation that *P. argentipes* has a much wider distribution than is at present known', and this author himself has recorded *argentipes* from Bombay, Saharanpur, Poona, Nagpur, Chhindwara, Karnal and Ceylon, places in which kala-azar does not occur. It may readily be admitted that there may be some other factor which enables the sandfly to prove a vector in one region but not in another. If climate alone be that factor, the absence of the disease from Bombay and from Ceylon where *argentipes* have been found up to a height of 1,500 feet above sea-level is very difficult to understand. In Ceylon, this is especially so, for the islands almost linking Ceylon to the south-east coast of India are heavily infected, and, according to Turkhud *et al.* (1926), coolies from Pamban and Mandapam in these islands have for many years gone to work in Ceylon.

In 1922 Patton stated

'In George Town (Madras) the number of sandflies is very limited, the only species being *P. minutus*. I have made many attempts to collect these flies from George Town but have never been able to get them,

and the people do not seem to know them : they must therefore be scarce and could hardly account for the many cases of kala-azar which occur annually.'

In 1926 Barraud found *P. argentipes* in the great majority of houses in George Town during a flying visit lasting a fortnight. Either, therefore, Patton who worked in Madras for several years failed to identify *P. argentipes*—a most unlikely occurrence in so eminent an entomologist—or *argentipes* have only recently reached Madras, though the disease had been endemic for many years before Donovan made his discovery of the parasite there in 1903.

In 1927 Savage reported two cases of kala-azar in boys who had almost certainly acquired the disease at Sanawar School. (a military institution for the children of British soldiers, situated in the Simla Hills). A careful search for sandflies made at that time revealed only *P. major*. Some six months after these cases had been reported Sinton (1927) wrote—

'In a collection of flies from Sanawar village kindly given me by Captain P. J. Barraud, F.E.S., F.Z.S., there were several specimens of this species . . . up to the present *P. argentipes* has not been recorded in the north of India west of Saharanpur . . . and our previous knowledge led us to believe that this species was limited to altitudes below 2,000 feet . . . although several thousands of this genus have been examined during the last seven years from areas within a few miles from Sanawar this is the first record of *P. argentipes* from that neighbourhood.'

It should be noted that Sinton himself worked for many years at Kasauli, only three miles from Sanawar School. Furthermore, *P. argentipes* were never found at Sanawar School but at Sanawar village, about two miles distant from the school by road and half a mile as the crow flies, and out of bounds for the school children.

This discovery by Barraud was hailed as further evidence of the close relationship between *argentipes* and kala-azar, although the sandflies were never found in the school where the cases of kala-azar occurred. Further, it should be noted that these cases occurred several years before Barraud's discovery, and during the period of Sinton's unsuccessful attempts to find *argentipes* in the neighbourhood of Sanawar. Again, a point so far overlooked is that the original case in the school was imported from Madras as reported by Bouché (1926), and Savage's cases might well have been infected by contact rather than by non-existent *argentipes*.

In support of the probability that contact infections are not uncommon, it may be noted that many workers have stressed the importance of intimate social intercourse in the spread of the disease. Thus, Rogers (1914) pointed out that European planters who had sexual intercourse with infected women acquired the disease, but that married planters living with their wives escaped. Korke (1913) who was on special duty on the kala-azar inquiry in Madras, state ' . . . kala-azar is a household infection . . . it appears to me that for the appearance of a fresh case "contact" with a previous case is necessary . . . ; its tendency is to run in the

same nationality'. Korke publishes a table showing how in ten streets of Madras kala-azar was more or less restricted to Anglo-Indians though others shared these streets. Michael (1926) devotes the whole of his publication on kala-azar in Pusa to showing how close personal contact appears to be the main factor in the transmission of kala-azar.

If kala-azar is a disease transmitted by an insect with a very limited range of flight, the disease should creep from house to house. Michael (1926), who appears to be the only worker who charted the disease in order of sequence in a newly infected centre of restricted area, has published two maps which throw light on this point. A close study of these maps (they require a hand lens) will show that the first ten cases of the disease occurred in a most haphazard manner both at Pusa and Maheshpur village. Barraud (1926) correlated the presence of *argentipes* with cases of kala-azar occurring in Madras. His sketch maps of Davidson and Uttakapan Streets show that kala-azar does not tend to creep from one house to the adjoining house. In Uttakapan Street (if the circle denoting an old history of kala-azar be taken as the original source of the disease) it will be seen that flies traversed three and then a further seven blocks of buildings in one direction and nine blocks and across the road in the opposite direction to cause infection, but they never infected people in adjoining houses or those living directly across the street.

It would appear that too much stress has been laid upon an alleged correlation between the distribution of *P. argentipes* and kala-azar. Ever since the sandfly transmission theory came into favour, diligent search has been made for this insect wherever cases of kala-azar have been reported, and with a high degree of success. Were equal diligence employed in areas where kala-azar is not present but where climatic conditions appear to be favourable to the sandfly, it is probable that an equal degree of success would be obtained, and the alleged correlation between the distribution of *argentipes* and kala-azar would disappear. Further, the observations of two eminent entomologists carried out during many years, Patton's in Madras and Sinton's in Sanawar, suggest that kala-azar can be present in the absence of *P. argentipes*.

(2) *Age incidence*.—As all authorities are agreed that there is a definite age incidence in the disease as seen in India, detailed references need not be given. Kala-azar is almost unknown under the age of two years; it is comparatively rare under five; it is commonest between the ages of six and twenty; and after thirty liability to acquire the disease diminishes. This age incidence does not suggest a biting insect. In insect-borne diseases, infants and children under five years of age are commonly the greatest sufferers.

(3) *Sex incidence*.—It is somewhat surprising that those favouring an insect-borne theory of

the disease should be unwilling to admit any sex incidence in kala-azar, though in view of Archibald's early recording in the Sudan (Archibald, *loc. cit.*) that the extreme rarity of the disease in females made it unlikely to be insect-borne, more attention should have been paid to the point.

Napier, who was mainly responsible for epidemiological studies of kala-azar in India, does not actually deny a sex incidence of the disease—he is more inclined to ignore it. Although he found that 76 per cent of cases attending the Calcutta School of Tropical Medicine were males and 70 per cent of patients in Assam were males, he briefly dismisses the subject with the pronouncement that females are more reluctant to come to hospital than males, and concludes 'I am not satisfied that the Calcutta figures indicate that more males than females become infected' (Napier, 1926).

The statement that women are more reluctant to go to hospital than men is least likely to be true of a disease such as kala-azar. Specific treatment is available and this has reduced the mortality from more than 90 per cent to less than 10 per cent. It is a household disease, and no woman is going to be content to die or to let her daughter die at home while her husband and son are being successfully treated at hospital. Furthermore, if the sexes really suffered equally from kala-azar and the high proportion of males to females seen in hospital were mainly due to selection, one would expect a correspondingly higher proportion of females in private practice. Brahmachari (1928) states that 90 out of 120 cases seen by him in private practice were males, i.e. almost exactly the same proportion as in hospital cases.

Korke (*loc. cit.*) found that there were 184 male to 86 female cases amongst Eurasians in Madras. Anglo-Indian females will enter hospital just as readily as males.

Michael (1926a) recorded deaths ascertained by a house-to-house inquiry at Maheshpur. As deaths alone were recorded and patients had not to face examination there could have been no point in the villagers deliberately misleading him. Michael recorded 27 males and three females.

Numerous other examples could be quoted from the literature, but the figures of McCombie Young on the subject are so conclusive that a reference to them alone should convince the unbiased reader. The following table showing age and sex incidence has been compiled from his book 'Kala-azar in Assam':—

	Under 1 year, M/F	1-5 years, M/F	5-10 years, M/F	10-15 years, M/F	15-20 years, M/F	20-30 years, M/F	30-40 years, M/F	40-50 years, M/F	Over 50 years, M/F	Total M/F
	9/9	1,530/965	4,786/2,710	4,412/1,513	3,392/1,258	2,758/1,054	2,065/483	1,900/361	138/44	20,324/8,669
Proportion of M/F.	1 : 1	1.6 : 1	1.7 : 1	2.8 : 1	2.7 : 1	2.6 : 1	4.3 : 1	5.1 : 1	3.1 : 1	2.3 : 1

If McCombie Young errs at all, it is in under-estimating the evidence indicating a marked sex incidence in kala-azar. He writes 'It is known that a certain number of better-class females do not appear for treatment in public owing to their being "Purdah nashin" but this custom is not very strictly observed in Assam, and it is unlikely that more than half the kala-azar-infected women among the unsophisticated villagers, who form the bulk of the cases, remain untreated in spite of the compulsory treatment regulations. Furthermore, if this special custom were the only cause of the difference, one would expect to find it absent in the age groups under ten, for before puberty the boys and girls of an Assam village are equally free in their movements. The difference is, however, still noticeable at those ages and this seems to indicate

that there is actually a greater liability to the disease in males, although it is probably not as great as indicated by the figures 70 and 30 per cent for which the reluctance of females to come forward for dispensary treatment probably accounts in part'.

How small this 'part' must be shown by the following facts:—

(a) Treatment was compulsory (McCombie Young, 1924). 'The name of everybody in the infected and contact camps was recorded on a roll which was checked by inspecting officers of the Sanitary Department, and for reporting any infraction of the rules by migration the village headman was paid an allowance.'

(b) The Commission enjoyed the entire confidence of the villagers who themselves knew and dreaded the disease (McCombie Young, 1924). 'These regulations were in entire accordance with public opinion, which operated powerfully to enforce them. For instance, with a certificate giving a free bill of health to the family, no girl from such a village could marry outside of it, nor indeed would others buy rice or fowls or other produce from a segregated village.' After commenting on the behaviour of the villagers, which was beyond praise, McCombie Young states 'the explanation lies in the well-founded dread of the disease in the minds of the Assamese'.

(c) If shyness played a part in preventing women from coming for treatment, it should be most marked in young women between 15 and 30 years of age, but the difference is even more marked in those of later years.

McCombie Young's findings have never been refuted. If any doubt remains, final proof that the disease is three times commoner in males than in females is supplied by Acton and by Napier himself. In a study of post-kala-azar dermal leishmaniasis these authors (Acton and Napier, 1927) stated—

'Females predominate relatively amongst patients suffering from the early lesions (depigmentation of skin); this is natural as the slight disfiguring effect of these lesions would not be as serious a matter to a man as to a woman.'

Yet in their series of 44 cases suffering from this disfiguring complaint in all its stages, 33 were males and only 11 were females.

Though we are not concerned with kala-azar in China at the moment, it is worth while noting

that the disease there seems even more restricted to males. Cochran (Brahmachari, *loc. cit.*) noted the disease in 84 males and 4 females. Patton and Hindle (1926) state 'from local information from residents who have some knowledge of the disease we gather that the disease is distinctly commoner in males'. Recently Dr. Cheng, Director of Public Health, China, told one of us that kala-azar was not a problem affecting women in China and asserted that this was certainly not because the disease was in any way hidden by females.

(4) *Race incidence*.—The same reluctance to admit a race incidence is again evident in Napier's words (1926):

'One may say that the racial, religious and caste distribution of the disease is fairly even; under certain circumstances one class predominates and under different circumstances another, so that any argument based on the observation of the predominance of any class amongst the patients of one locality will be unsafe unless the special conditions in that locality are taken into consideration.'

Napier himself found that the disease was more prevalent in Anglo-Indians, Indian Christians and Mohammedans than in Hindus, and wherever the disease has been studied in India this has been a constant finding. The most striking examples of race incidence is supplied by Turkhud *et al.* (1926) from whose table the following figures have been compiled:—

	Mohammedans	Hindus	Indian Christians
Total population ..	23,925	25,389	2,155
Number having kala-azar	147	19	50
Percentage of infections	0.61	0.07	2.31

It is so generally accepted a fact that Anglo-Indians, Indian Christians and Mohammedans suffer more from the disease than Hindus that it is not worth while labouring the point. One more instance however may be cited for the sake of refuting the ingenious reply brought forth. At the Seventh Congress Meeting of the Far Eastern Association of Tropical Medicine held at Calcutta in December 1927, Lieut.-Colonel Ross (then Director of Public Health in Bihar) stated that in a detailed survey of kala-azar in Patna, Mohammedans were found to suffer far more from kala-azar than Hindus, and declared that no biting insect could distinguish between a Mohammedan and a Hindu. In the discussion that followed Knowles (1927) admitted that this had also been noticed in Calcutta, but added that nearly all the Hindus in north Calcutta kept cows and that Lloyd and Napier had shown that *P. argentipes* would feed every time by preference on bovine blood. This explanation, regardless of the fact that in a crowded city like Calcutta few Hindus can keep cows, appears to have satisfied the Commission. That it is not a satisfactory explanation is shown by Bentley and McCombie Young. Bentley (1914) who claimed to have seen a very large number of cases in Assam stated: 'In the infected lines there were very old coolies and they had been allowed to have very much their own way, with the result that they kept cattle in the verandahs of nearly every house. In the healthy lines cattle were not allowed to be in the verandahs of houses; there were cattle-sheds and all cattle were stabled apart from the dwellings'. Further proof that cattle do not afford any protection was given by McCombie Young as long ago as January 1914. He found that no less than 76.8 per cent of those suffering from

kala-azar in Assam kept cattle (McCombie Young, 1914).

To recapitulate: the age incidence, sex incidence and communal nature of the disease together with other epidemiological observations mentioned in this paper cannot be reconciled with the theory of transmission by a biting insect.

We find ourselves unable to envisage an insect with such peculiar propensities in biting that it will avoid the tender skin of the infant, that it will attack the tougher male in preference to the more delectable female: that it will select members of one community and neglect members of other communities living in the same environment, in the absence of any evidence that conditions among the communities (selected or neglected) are such as might be expected to encourage or deter the breeding of the insects.

Now compare this observation of Christophers (1926) with the experience of the Yellow Fever Commission in Cuba. 'Whilst feeding sandflies, members of the Commission spent many occasions both by night and day sitting or reclining on the mud floors of these (kala-azar) huts, but have never had occasion to repent their rashness in this respect.'

How does the sandfly transmission theory account for the following epidemiological observations?

(1) The disease is rural rather than urban: in cities it occurs more frequently amongst those living in masonry houses than in mud huts. Yet the sandfly is a house-dweller seeking cracks and crannies in walls and is not found breeding in vegetation.

(2) 'Old' coolies ('old' by length of residence not in years) are more susceptible than newcomers (Price, 1923).

(3) The failure of the disease to spread in Ceylon where *argentipes* have been found up to a height of 1,500 feet above sea-level, where climatic conditions appear to be suitable and where the disease has been frequently imported from neighbouring islands.

(4) The failure of the disease to spread in schools and hospitals although it is a house infection.

We stress these points to refute a recent textbook statement: 'So far as India is concerned every epidemiological observation fits in with the sandfly hypothesis of transmission' (Napier, 1943).

The supporters of the sandfly transmission theory place great emphasis on two points:—

(1) All other theories leave out of account the fact that the parasite flagellates in an invertebrate host and, on analogy, that host must play a part in the transmission of the disease.

(2) Kala-azar has a strictly limited geographical distribution which calls for a more complicated biological process than direct contact for its transmission.

The first is the argument of the biologists and has already been dealt with.

### Geographical distribution

It is hardly true to say that the geographical distribution of kala-azar is so strictly limited that an insect vector must be necessary for its transmission. Kala-azar has indeed a wide distribution over areas in three continents showing great diversity of climate. That we do not yet know its limits is evidenced by the discovery of endemic foci in East Africa and South China, and by the appearance of cases in Abyssinia a few years ago. Further, there are other diseases with a distribution just as limited, e.g. yaws and undulant fever, in which an insect vector plays no part.

Sufficient attention has not been paid to the skin in kala-azar. The word itself means 'black sickness' and the pigmentation, which is characteristic of the disease, suggests early involvement of the cutis—a suggestion now conclusively proved by Kirk and Sati (1940) who have reported the presence of *Leishmania* in the skin of 57 per cent of ordinary cases of kala-azar in the Sudan. This was demonstrated by smear examination alone and did not include cultural methods. According to Manson-Bahr (1935)—

'Hu and Cash have made the most interesting observation that the Leishman bodies are taken up by the cells of the reticulo-endothelial system or clasmato-cytes, and in experimentally infected hamsters become massed as a thick layer of heavily infected tissue immediately underneath the skin, though externally no change can be seen on the surface of the body. This observation has been confirmed by Hindle. In skin-sections from a fatal case of kala-azar, a similar condition was seen. All levels of the skin below the epidermis contained leishmania-filled cells collected in large masses about the sweat glands and arterioles and scattered diffusely throughout the corium.'

These observations lend support to those of earlier observers in the field that the transmission of kala-azar depends on close contact and intimate social intercourse between infected and non-infected human beings. Leishman-Donovan bodies are probably always present in the skin: they have been found in faeces, urine and nasopharyngeal secretions. Chinese hamsters can infect one another by contact. All are agreed that oriental sore is easily transmitted from one person to another by 'vaccination', and that auto-inoculation is a not uncommon occurrence. On the other hand, all experimental methods of transmitting kala-azar and oriental sore by means of the sandfly have been attended by very considerable difficulties, and so artificial have been the conditions that not until now has any author dared to claim that infections normally occur by such means.

We venture to suggest that the supporters of the sandfly theory of transmission have been carried away by the results of laboratory experiments, have not paid sufficient attention to the study of the fly in nature and have ignored or denied the mass of epidemiological evidence which casts grave doubt on the correctness of their theory.

The old-fashioned idea that intimate contact is necessary for the transmission of kala-azar needs to be revived and further investigated. Equally important factors requiring investigation would appear to be—(a) Abrasions: which may account for the greater incidence of the disease in males, its predominance in rural areas rather than crowded cities and the fact that children suffer more from the disease than infants. (b) Constant sweating: suggested by the pathological involvement of the sweat glands and the fact that the disease flourishes most in India, in those regions where constant sweating, day and night, is marked throughout the summer months when infection is most commonly acquired. (c) Lack of personal cleanliness: suggested by numerous observations that the disease is most marked in communities that pay least attention to personal hygiene. Thus the poorer classes of Hindus on whom customs and religion enjoin a fair degree of personal cleanliness suffer to a less extent than Mohammedans and Indian Christians. This may even be the reason why the disease has never spread to Burma and Ceylon, for the peoples of these places are well known for their love of bathing. [In this connection see investigations on the auto-sterilizing ability of the clean skin quoted by Topley (1933).] We put forward the plea that these factors be further investigated and that judgment be suspended by those who are inclined to favour the sandfly transmission theory.

[Note.—The above article is published not because the editor agrees with all that is said in it (for he does not), but because it outlines the many points about the transmission of kala-azar which are still far from clear and of which further investigation is necessary. He hopes that this article may call forth a reply from those who have made a special study of the subject and who have real evidence against the opinions expressed.—EDITOR, I. M. G.]

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## THE TREATMENT OF MENTAL DISORDERS BY ELECTRICALLY INDUCED CONVULSIONS

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IN the field of mental disorders, failure to plan therapeutic experiment has led to much confusion. Cardiazol, insulin, electrical convulsions and leucotomy have come to the stage in turn, but there is still controversy about their efficacy and the indications for their use. Convulsion therapy in some form is now in common use in the majority of modern mental hospitals all over the world. In the mental hospitals of Ontario, 1,600 patients were given 'shock treatment' during the years 1938-41, and the statistical report concludes, 'it is safe to assume that in consequence of the shock therapy work carried out during the years 1938-41, there were fewer patients on the books of the mental hospitals of Ontario during the year 1941-42, than there would have been if no such specific treatment had been given'. This statistical report definitely proves the utility of 'shock therapy' in mental hospitals. When I was in Budapest in 1935 I learnt the cardiazol shock therapy from Dr. Ladislaus V. Meduna, the originator of cardiazol therapy. On my return to India in 1936, I introduced this therapy in the Ranchi Indian Mental Hospital, and since then it has been in use in the majority of the mental hospitals in India with encouraging results. I have, up to date, treated more than 500 cases of mental disorders by cardiazol therapy without any fatal accident. Fractures, specially of the spine and long bones, have been cited as frequent complications in cardiazol therapy, but my experience must have been happier than that of some other psychiatrists, as I cannot recall more than four fractures and about 20 dislocations in my series of over 500 cases, each case having received at an average 12 shocks by cardiazol. I also feel bound to mention that I have observed no signs suggesting that cardiazol therapy had injured brain tissues. I am fully convinced that 'shock therapy' must be tried in all early as well as late mental disorders before the case is given up as hopeless. I have fully narrated my experience of 'shock therapy' by cardiazol in my articles in the *Lancet* and the *Indian Medical Gazette*, and it is my aim in this paper to describe in full my own experience in the use of convulsion therapy by electric apparatus. This is the first time such an apparatus has been used in India.

*Origin of electric shock therapy.*—In 1938 Cerletti and Bini of Rome reported that convulsions



could be induced by the passage of an alternating current across the frontal region, and they developed a technique for the application of this method to replace convulsant drugs. In England, Fleming, Golla and Walter (1939) carried out similar experiments and demonstrated that electric convulsant therapy provided a safe and simple method of inducing convulsions.

We used the MacPhail-Strauss apparatus. This apparatus, constructed on the principles laid down by Cerletti and Bini, but with important modifications, has been evolved after two years' work at St. Bartholomew's Hospital, London, by Strauss and MacPhail (1940).

*The apparatus provides :—*

1. Means of operation on any voltage between 200v and 250v A.C.

2. A means for measuring the patient's transtemporal resistance by means of an alternating current resistance circuit.

3. A means of providing a convulsant shock of any given voltage between zero and 150v applied to the patient for a definite fraction of a second controlled by an electronic time-switch.

4. Two electrodes to be applied on each side of the head with a rubber bandage to hold the electrodes and two pieces of rectangular sponge.

*Supply.*—The apparatus is designed to work on alternating current only, but it can be worked on direct current with a motor convertor and autotransformer.

*Preparation of patients.*—I have always taken care to make the treatment seem to the patient very much a matter of course. In fact too meticulous a preparation may induce apprehension in the patient and he may resent the treatment.

The patient is allowed only a cup of coffee or tea in the morning at 6 a.m., and is not allowed to take any other food or drink at all until three hours after the shock. The shock is generally induced at about 9-30 a.m. so that he is usually able to have his lunch at midday, three hours after. Even a small quantity of food in the stomach may be regurgitated and inhaled during the shock, and the above precautions are necessary to avoid this possibility. The bladder and rectum should be emptied before the shock. The patient lies supine on a wooden plank bed with a hard mattress. This is preferable to a spring bed. The patient's clothing is loosened, and hair pins, false teeth and spectacles or metallic objects are removed. The skin and hair of the temporal areas are thoroughly cleansed with ether soap and warm water to remove all hair dressings and skin secretions. This is very necessary. I have often found considerable difficulty in the passage of currents in my Indian patients as they generally bathe their heads with oil and therefore require thorough cleansing as the passage of current is obstructed by greasy substances. Sometimes we had to clean the patient's head more than once, as the current would not pass on account of oil-stained

electrodes. A 20 per cent saline solution is well rubbed into the skin and hair, and the electrodes are applied one on each side of the head over the pre-auricular and supra-zygomatic part of the temporalis muscle, two intervening layers of lint soaked in 20 per cent saline being placed between the skin and each electrode. To ensure perfect configuration of the electrodes on the side of the head, the electrodes are held in position by a 3-inch rubber bandage applied over the rectangular sponges, which are also soaked in 20 per cent solution of saline, the whole assembly pressing the electrodes and lint closely to the side of the head.

The next part of the procedure is to *measure the patient's 'transtemporal resistance'*.—This is done by setting the galvanometer. The point indicated in the resistance circuit at which the galvanometer is 're-balanced' is the patient's transtemporal resistance. The measuring of transtemporal resistance is fully explained in the instruction booklet supplied with each apparatus, so that it is not necessary to go into any further detail here. The transtemporal resistance is some guide in estimating the voltage of the current but of great value to the operator as regards the passage of current; as, for example, if the patient's T.T.R. exceeds 1,000 ohms, the galvanometer needle will not 're-balance', and this indicates that the skin has not been thoroughly prepared and the electrodes should be removed and the cleansing process repeated. We had to do this frequently in the case of Indian patients as their hair was excessively oily.

*The shock.*—The patient is now ready for his convulsant shock. All machines in common use deliver a 50-cycle alternating current, from the A.C. mains, of 200 to 240 volts, and the duration of the exposure of current should be from 0.1 to 0.5 second.

*The average time exposure of current.*—I have always adhered to 1/10 of a second. The current which flows through the patient's head is of the order of 0.5 to 1 ampere. The shock is therefore of such a size that if passed through any part of the body other than the head it would be highly unpleasant. If a shock of this size were to pass through the heart, it would end fatally, yet not one patient in thirty was aware of having received an electric shock. The reason for this is to be found in the size and positions of the electrodes and the resultant current distribution. The electric convulsion method evolved by Cerletti and Bini is based on the well-known effects of electrical stimulation of the cortex. When the cortex is exposed at operation and direct stimulation is applied, it is found that a current of about 10 milliamperes is usually required to produce a maximal response. From measurements taken on the outside of the scalp it has been shown that the normal electrical sensitivity of the cortex is attenuated as much as a hundredfold by the overlying tissues. It

follows therefore that to produce a stimulus of 10 milliamperes through the motor cortex, a current of approximately 1,000 milliamperes should be passed through the skull in the frontal region.

As Cerletti and Bini found in the earlier stages of their work, the current passing through the head is not proportional to the applied voltage, i.e. Ohm's Law does not apply.

This is due to the fact that the greater part of the head resistance lies in the skin and superficial tissues which undergo a temporary change during the passage of a strong current. The nature of this change is not fully understood, but it tends to reduce the effective resistance. The practical significance of this is that a lower voltage is required to provide a maximal stimulus to the cortex than would be expected from the observed resistance of the head between the electrodes.

*How to determine the appropriate voltage and exposure time for each patient for giving shock by electric apparatus.*—The convulsive threshold varies in different patients, and cannot be predicted, and the only way to begin a course of treatment in a given case is to use a standard medium course. Experience has taught us that for an average size of Indian patient it is advisable to begin with 90 voltage, the duration being 1/10 of a second. If a shock was not induced by 90v, I increased it to 100v, and the majority of my Indian patients got a shock with this voltage. With European patients the average working voltage, I found, was between 100 and 105v, the time being 1/10 of a second. In a few cases I had to go up to 115v, but I have never exceeded this limit, as in every case in our series a fit was induced with 115v as maximum and 90v as minimum. If the fit occurs immediately at a given voltage, the same voltage may be used next time. If after the shock the convulsion is delayed, say from 3 to 30 seconds, it means that the voltage is not strong enough to produce convulsion, and the voltage must be increased next time. There is always a small progressive rise in the convulsant threshold after each of the first few fits. The increase may be either in voltage or duration. I generally prefer to increase the voltage and keep the same duration, i.e. 1/10 of a second. If no convulsion results at all after a given voltage, another stimulus must be given, at an increased voltage, and successive shocks are given until a convulsion is induced. In one patient I have given four such successive shocks with increased voltage each time. This shows that occasionally we may come across patients who may be extremely fit-resistant. It has been recorded by others that in some cases even the strongest and largest stimuli often failed to evoke a fit. In such cases electrical treatment should be discontinued and cardiazol may be tried. I have come across such fit-resisting patients with cardiazol therapy also. No patient should be given a second shock

unless he has completely recovered from the effects of the first.

*The value of transtemporal resistance (T.T.R.).*

—It is advisable in every case to take the T.T.R. by the galvanometer attached to the apparatus. I admit that there is no established correlation between resistance readings and the convulsant threshold. Experience shows that often a low-resistant patient needs higher currents. In my series, some patients with T.T.R. as high as 1,000 were convulsed at 90v, whereas other patients with low T.T.R., i.e. 300 to 400v, could not be convulsed with as high as 105v. This indicates that there is no correlation between T.T.R. reading and convulsant threshold. In my opinion the transtemporal reading is necessary to make sure that the electrode contact is good and that the electrodes are not frayed or broken. I have never succeeded in evoking a fit with a T.T.R. over 1,000. This shows that there was some fault in the circuit of the current from the mains to the electrodes, and at times we had to open up and clean the electrodes and the patients five times or more before we could evoke a fit. This is the only value of T.T.R. readings.

*The fit.*—As soon as the current is switched on, the shock causes instantaneous unconsciousness, and a major fit is evoked. This fit is associated with a tonic convulsant phase which lasts for a few seconds and passes gradually into full clonic contractions, which, after some 20 to 30 seconds, die away and give place to a phase of exhaustion-relaxation from which the patient gradually recovers consciousness.

The reappearance of consciousness occurs some 4 to 5 minutes after the shock, and is associated with disorientation and amnesia which, however, rapidly clears in some minutes except for short retrograde amnesia which extends for some minutes before the actual shock. This latter is permanent and is, in fact, an advantageous feature of the treatment and contrasts favourably with chemically induced shock.

It is advisable to remove the electrodes and headgear from the patient's head before he regains consciousness, as their presence might be disturbing on waking.

*Complications.*—One occasionally comes across circulatory and respiratory complications during a fit, and occasionally there may be dislocations and fractures, although these complications are far less frequent and less severe than in cardiazol shock therapy. In my series of 30 cases, I met with 2 dislocations of the jaw which were set right immediately and before the patient regained consciousness.

*Is electric shock therapy a great advancement on cardiazol shock therapy?*—I have acquired considerable experience in cardiazol therapy, but I must admit that, given a choice, I shall always prefer the electric method, both from the standpoint of the patient as well as the doctor. The electric shock therapy is commended because of the ease of operation, the

freedom from special disadvantages inseparable from the use of a blood-borne drug, and the accuracy of dosage which it is possible to obtain.

The disadvantages of cardiazol therapy are :—

(a) There is a feeling of terror induced in the patient while the dose is taking effect. This is frequently such as to deter the patient from undergoing any further treatment, and generally the patients describe the sensations following injections as a feeling of impending death.

(b) In certain cases it is difficult to inject the drug into the vein, and if injected intramuscularly there is an abnormally long interval before the reaction is obtained.

(c) Patients at times object strongly to intravenous injections.

(d) The greatest triumph of electric therapy over cardiazol is the amnesia of events surrounding the actual shock. The patient remembers the process as far as the tying up of his head with the electrodes, but as soon as the current is applied he becomes unconscious, and remains so till he completely recovers from the fit. On recovery he has no memory of what has taken place.

On many occasions, patients after the shock have asked me when I was going to start the treatment, and they have often doubted my statement when I assured them that I had already given it to them. This complete loss of memory of events is no doubt a great blessing to the patient and a notable advance on cardiazol therapy where the patient remains in complete dread of the treatment.

*Results of electric shock therapy.*—The 30 patients in my series could properly be called recent cases. None were chronic invalids, as mental illness in every instance had been in existence for less than a year. Our results have been judged as recovery, improvement, or no improvement. Those patients who were free from psychotic symptoms were classed as recovered. Patients who fell short of complete recovery, but in whom sustained change for the better was reflected by their conduct and behaviour, were classed as improved. Patients who showed no improvement were shown as such. Of the 30 cases, 28 were males and 2 females.

The following table shows the results of electric convulsant therapy :—

		Number of cases	Recovered	Improved	Not improved
1. Schizophrenia	..	13	4	5	4
2. Mania	..	4	3	1	..
3. Depression	..	10	8	1	1
4. Psychoneurosis—					
(a) Hysteria	..	1	1	..	..
(b) Anxiety neurosis	..	2	1	1	..

As will be seen from the above table cases have been classified in four diagnostic groups.

The schizophrenic groups have not been subdivided.

1. *Schizophrenia.*—Of the 13 cases 4 recovered, 5 improved and 4 showed no improvement.

(a) An officer was suffering from schizophrenia, and was considered a hopeless case. He had been given six cardiazol shocks with no effect. He was given 12 electric shocks, and he made a marvellous recovery.

(b) A Polish refugee girl with schizophrenia was treated for four months with cardiazol and other methods without any good result. She was given 12 treatments by electric convulsant technique, and she made a very quick recovery and was discharged to her camp as fully recovered.

Of the 4 schizophrenics that did not show any improvement, 2, after three shocks, refused to have any further treatment, and we could not compel them to take the full course. The remaining 2 were given full courses.

2. *Mania.*—Of the 4 patients with mania as the main symptom, 3 made a good recovery and 1 improved under treatment.

3. *Depression.*—Of the 10 depressive cases, 8 recovered, 1 improved, and 1 did not improve under treatment.

(a) A patient with acute depression of the manic-depressive psychosis type, made a remarkable recovery after 12 shocks.

This kind of affective psychosis recovers well both with electric therapy and with cardiazol therapy. In fact shock therapy, whether by electricity or drug, can almost be regarded as of higher value than any other form of treatment in affective psychosis, especially 'depressions'.

(b) A case of stuporous melancholia on the 'seriously ill' list for two months, and fed nasally, made a speedy recovery under electric therapy. He was only given 5 shocks, and though very weak he was able to stand the shocks. I could not have taken a similar risk in view of his extremely weak physique, with cardiazol therapy.

It appears that the electric method of shock treatment is capable of use in cases where the age, the mental and physical conditions of patients prohibit other shock methods of treatment. This therapy can also be used in those with marked excitement. In such a case, a sub-shock is given to make the patient temporarily dazed, and is followed immediately by a shock of voltage effective to evoke a fit; e.g. if a patient is highly excited he is given a sub-shock of, say, 80v, which stuns him and so causes him to relax. This should be followed immediately by, say, 100 to 105v. An excited patient can also be rendered quiet by premedication with morphia, hyoscine, paraldehyde, etc., but I prefer the sub-shock method. I have given such treatment to highly excited patients with gratifying results.

4. *Psychoneurosis.*—Of the 3 psychoneurotics, 2 recovered and were discharged to duty and 1 improved.

Thus, the results of electric shock therapy were extremely encouraging in our series of cases. Use of this therapy has shown that it can benefit many kinds of mental disorders. It is not of

value in schizophrenics where delusions and hallucinations are prominent, and in such cases the consensus of opinion is in favour of insulin therapy. Electric therapy is very valuable in the katatonic and depressive phases of schizophrenia. Mania, depression, involutional melancholia, and psychoneurosis of recent origin respond well to this type of treatment, and it should always be tried in these cases.

*How to fix the number of shocks to be given in each case and how often in a week.*—The maximum number of shocks given to patients in the series was 12, and the minimum 3. As to the number of shocks to be given, in each case I was guided by the nature of improvement taking place. If a patient shows marked improvement after 5 or 6 shocks, it is my routine to give 2 more shocks before stopping the treatment. Generally shocks are given three times a week, twice a week or every day, dependent entirely on the physical health of the patient. The majority of patients in the series received shocks three times a week. If a patient showed no improvement of any kind after 9 shocks, treatment was discontinued.

*Contra-indications for treatment.*—Every patient must be thoroughly examined physically before he is passed fit for treatment. The following diseases are considered contra-indications for treatment:—

- (a) All heart and lung diseases.
- (b) All fevers.
- (c) Organic diseases of the brain and central nervous system.
- (d) Any important bodily affection.
- (e) Sugar and albumin in the urine.
- (f) Age is not itself of great importance provided the subject is physically fit. Shocks have been given to children of 3 years, and old men of even 80 years.

*Comments.*—In the series of 30 cases, I met with no fractures, but in 2 cases I had to reduce dislocation of the jaw, which occurred with the first shock. With adequate precautions, however, there was no recurrence with subsequent shocks.

Fifteen patients in the series complained, after each shock, of defect of memory, both recent and remote, which cleared up within a few

hours. In one case the patient had a marked loss of memory, being unable to recognize his friends or family for two days, and living a vegetative existence. His memory invariably returned after the third day, and he behaved like a normal person. He showed this behaviour after every shock. After the last shock he lost his memory for nearly a fortnight, but it returned after this period, and he became quite normal again. This peculiarity of the loss of memory was noted in this case only.

*Summary.*—1. Electrically induced convulsant therapy has been fully described and discussed.

2. The results of 30 cases treated by electrical stimulation of the brain have been analysed, and the results were extremely encouraging.

3. This treatment is highly satisfactory in affective psychosis and psychoneurosis. In illness of recent origin its effect is much more favourable, but it is of great value in securing some improvement in the behaviour of chronic cases also.

*Acknowledgments.*—I should like to acknowledge my appreciation of the valuable help I have received from Mr. H. J. Wright, who very kindly set the apparatus in working order for me. I am also indebted to Brigadier E. A. Bennet, Consultant in Psychiatry, India Command, for supplying me with all the literature and notes on this therapy.

I am also grateful to the officers commanding British and Indian General Hospitals of my area for their help and encouragement. I am equally grateful for the valuable help I have received from the medical and nursing staff of both the hospitals.

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## Medical News

### THE ANNUAL GENERAL MEETING OF THE ASSAM AND NORTHERN BENGAL BRANCH OF THE BRITISH MEDICAL ASSOCIATION HELD AT SHILLONG ON THE 4TH, 5TH, 6TH AND 7TH NOVEMBER, 1943

Dr. G. C. RAMSAY, M.D., C.I.E., O.B.E., in his presidential address discusses several points of interest including the use of Pyrethrum Bomb for spraying houses and huts, the value of suppressive treatment with quinine, the importance of *Anopheles leucosphyrus* as a vector of malaria in war zones, the use of cuprous cyanide as a larvicide, malaria control by shading and

flushing out streams during dry seasons. Dr. E. Burke in his paper on 'Medical Problems of Wartime Tea Estate Practice in Assam' covers a very wide field including housing, clothing, fuel, malaria, dysentery and diarrhoea, anaemia and dropsy, hookworm, cerebrospinal meningitis, kala-azar, paga sore, tuberculosis, ophthalmia, tropical neurasthenia in Europeans, food shortage and malnutrition. It is impossible to abstract this paper. Dr. S. R. Pandit gave an interesting account of the Assam Blood Bank. Colonel Shortt gave a résumé of research on kala-azar with special reference to Assam. Colonel Shortt's paper outlines the development of knowledge on this subject during the last 50 years, to which he himself has contributed

greatly. The summary is a very useful one. Major Jellison gave a demonstration of the Freon Aerosol Bomb; one bomb is said to spray 100,000 cubic feet effectively. An interesting discussion on malarial epidemiology and treatment clearly indicated the seriousness of the problem and the divided opinion on the aetiology and treatment. A resolution on the need for research on this matter was passed.

## TERMINOLOGY IN HUMAN MALARIA

(from IHD newsletter)

THE common English terms used to distinguish the various types of human malaria are confusing enough to American and British readers but they are especially annoying to foreigners, who feel that we should at least come to some agreement on them among ourselves. Americans do not use 'malignant tertian' or the English 'estivo-autumnal' (not even in the form 'æstivo'), and the meaning of 'subtertian' is not very clear to either, but all appear frequently in scientific articles. The names, based on the striking periodicity of clinical malaria, developed and took root during the centuries before its aetiology was known. They are among our most ancient medical terms, dating back to the fourth century B.C. when Hippocrates described periodic fevers as quotidian, tertian, subtertian and quartan.

In the meantime the respective organisms have been described and named: *Plasmodium malariae* by Laveran in 1881, *Plasmodium vivax* by Grassi and Feletti in 1890, *Plasmodium falciparum* by Welch in 1897, and *Plasmodium ovale* by Stephens in 1922. These names are now very generally accepted in English-speaking countries, although there is still some controversy in Italy and France over the 'malignant tertian' parasite known variously as *præcox*, *immaculata* or *falciparum*. The Malaria Commission of the League of Nations appointed a sub-committee in 1937, consisting of Christophers, Hackett, Sergent and Schüffner, to attempt to standardize malaria terminology and their report was published in the *Bulletin of the Health Organization* (Vol. IX, No. 2, 1940). The report states (p. 145) 'Though benign tertian and malignant tertian are the names now used by most English writers, and estivo-autumnal by many American authors, such terms are not only inappropriate and archaic, but also long and cumbersome. . . . The names *perniciosa* and *tropica* (often used by German writers) imply zoological names for the parasite which do not exist. Some authors use tertian, quartan and tropical for the parasites. . . . The sub-committee considers that it would be desirable to employ in place of such colloquial names as those given, the italicized specific name of the parasite referred to. Thus an infection by *P. vivax* would be a *vivax* infection, etc. The corresponding symbols [e.g. (V.) for *vivax*, (M.) for *malariae*, etc.] might be a little difficult to use at first, but once they became familiar would be as convenient as the present (B.T.), (M.T.) and (Q.) often employed'. However, in the latest edition (1942) of Stitt's *Tropical Diseases* (Strong) the parasites and their diseases are still referred to as benign tertian, quartan and malignant tertian (or estivo-autumnal).

The League report referred principally to the common names of the parasites and infections, but it is time to raise the question whether we should not carry the simplification a step further and apply the unitalicized name of the parasite to the disease itself dropping all the other names, at least for publication. Dr. Boyd recommended this at a meeting of the A.A.S. in 1940, suggesting only that for euphony the term 'quartan malaria' might be substituted for 'malariae malaria', as I think we all do in conversation.

Now comes an announcement in the *American Journal of Public Health* (editorial on p. 845 of the July 1943 number) that 'as an editorial policy, the journal will in the future attempt to be consistent in this matter and, so far as nomenclature is concerned, will blue-pencil all terms not in conformity with a terminology

based upon aetiology' namely: *vivax malaria*, *falciparum malaria*, *malariae malaria* and, presumably, *ovale malaria*. The staff of the IHD could do no better than to adopt this rule, also, in their publications.

LEWIS W. HACKETT.

Further etymological note: After considerable delving into the literature, corresponding back and forth, and discussing pro and con, it has been decided that *Hæmogogus capricornii* shall in future appear like that. Two 'i's', please.

## REFORM IN TERMINOLOGY

(from IHD newsletter)

IN the last Newsletter Dr. Hackett summed up the case for a simpler and better nomenclature for the types of malaria. The *American Journal of Public Health* had already announced its editorial policy to abide by the reform. Now we take pleasure in observing the following footnote in the *Journal of the American Medical Association* (18th December, 1943, page 1052) under a statement by the sub-committee of Tropical Diseases of the National Research Council:

'In the interest of more accurate diagnosis and better treatment, physicians are urged to use the aetiological terminology in differentiating the four malaria infections of man as follows: *falciparum malaria* (instead of estivo-autumnal, subtertian, malignant tertian, tropical or pernicious malaria), *vivax malaria* (instead of tertian or benign tertian malaria), *malariae malaria* (instead of quartan malaria) and *ovale malaria*.'

Another overdue reform in the designation of diseases would be the exclusion of the terms 'epidemic' and 'endemic' from the names. Misguided attempts have been made to have jungle yellow fever called endemic yellow fever, and to designate infective hepatitis as epidemic hepatitis.

Typhus nomenclature is likewise bedeviled by the use of the terms 'epidemic' and 'endemic typhus' for the classic and the murine types. We hope that epidemiologists will arise and fight the misuse of these very necessary words with so definite a technical meaning in their specialty.

## PROMOTION OF POSITIVE HEALTH

MEDICAL CURRICULUM MAY BE REVISED

IT is becoming increasingly recognized throughout the world that prevention of disease and the promotion of positive health require more emphasis than mere provision of measures for curing sickness.

The Health Survey and Development Committee has had under consideration the question of revising the medical curriculum so as to shed much of the unnecessary load that is placed on the medical student and of improving the content of the subjects taught and the method of teaching, particularly for the purpose of giving a preventive bias to the outlook of the student. The proposed changes in the curriculum will, it is hoped, enable the doctor of the future to offer to the people of India both curative and preventive health service in an effective manner.

Other subjects considered by the committee (which, with its sub-committees, held meetings between 1st and 15th July) included the place of the indigenous systems of medicine and of homœopathy in the future programme of medical relief for the country; the health of the school population; the control of venereal diseases; prevention of smallpox; physical education; health education and publicity; the problem of nutrition and control of food adulteration.

Groups of members of the committee will shortly undertake tours in the provinces of Delhi, the U. P., Bihar, Orissa, Bengal and the C. P. Industrial centres in Northern India will also be visited. These tours will complete the rapid survey of existing health conditions in British India by the committee, that has been in progress during the best part of few months.



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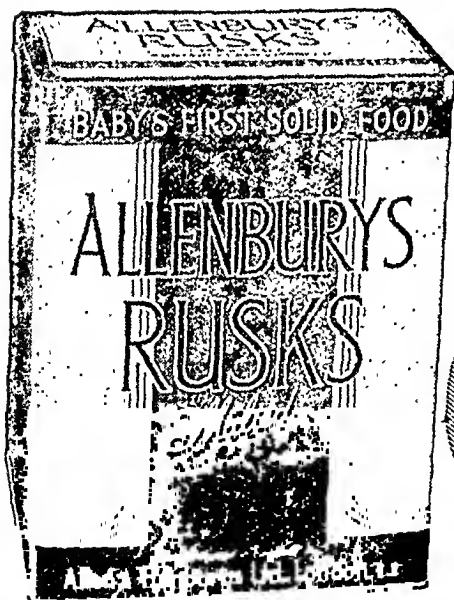
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## Public Health Section

### THE PREPARATION OF MANURE WITH NIGHT-SOIL AND STREET RUBBISH

By P. K. GEORGE, L.M.F., L.P.H.

Health Officer, Trichur

THE question of adequate supply of manure has jumped into prominence owing to the introduction of increased food production schemes consequent upon the acute scarcity of food-stuffs.

The low yield of crops is mainly due to the want of proper and sufficient manure to the land.

Farm-yard and green manures are chiefly used for agricultural purposes. The quantity available is not sufficient to meet the present demand.

The disposal of night-soil and street sweepings is a serious problem that faces every sanitarian. In the case of smaller towns where the arrangements for the removal of town refuse are primitive and the resources of the municipality are very limited, the problem becomes a nightmare to the municipality.

Night-soil and rubbish are articles of high manurial value. In fact these are the only sources of organic manure which can meet the qualitative and the quantitative requirements of agriculture. The only thing is that they are abhorrent to handle in their original form. In these days of acute food shortage when the slogan is 'grow more food', these articles have to be converted into manure that can be easily handled by the agriculturist and handed over to him in the shortest possible time.

The combined method of disposal of night-soil and street sweepings that is being used by the Trichur municipality at its disposal ground in Laloor is found to have the following advantages :—

1. It requires the smallest ground space for the operation.
2. It gives a manure that is biologically clean in the shortest possible time.
3. It is a very simple process and does not require any complicated apparatus.
4. It can be done in all seasons.
5. It is cheap and is within the reach of even a small village panchayat.
6. It can be done very near the town and causes little nuisance.
7. Experts are not required.
8. It produces double the quantity of manurial principles of farm-yard manure.

**Compost manure.**—A process of biological fermentation of bulky organic matter so as to convert the rubbish and night-soil into a new substance of high manurial value, within 7 weeks.

The process used in the Trichur municipality is detailed below :—

(1) *Sorting and heaping of rubbish.*—Rubbish is first sorted, and pieces of metal, glass, chips of wood, etc., are removed. This rubbish is then heaped in such a manner that there is a width of 5 feet at the bottom and 3 feet at the top with a height of  $2\frac{1}{2}$  feet, the length of heap depending upon the quantity of night-soil to be applied. A heap of 4 to 5 feet long is enough for a drum of 20 gallons of night-soil. The packing of the rubbish should be very loose. On such a heap of rubbish a trench of  $1\frac{1}{2}$  feet deep and 1 foot wide is made.

(2) *Emulsification of night-soil, mode of application and dosage.*—The night-soil is then made into a thick even emulsion adding the necessary water and stirring it with a churning rod. Water is found not necessary in winter. The emulsified night-soil is then spread evenly in the trench made on the top of the rubbish heap and covered over by drawing in the sides of the rubbish heap.

(3) *Raking and aeration.*—On the fourth day of the first application, the heap is thoroughly raked up with forks so as to admit plenty of air into the heap. This is quite important as the success of the process depends upon the speed of decomposition accelerated by increased aeration and turnings given to the compost mass.

*Ré-application of night-soil.*—On the seventh day, the heap is raked up again, and on the eighth day, after forming a trench on top as before, a second dose of night-soil emulsion is applied. In this way 7 applications are made when the rubbish heaps become saturated with night-soil.

It is advisable to re-heap the stuff before every application to secure homogeneity. After the last application, the heaps are allowed to lie over for 8 to 10 days to mature. Now it is ready for sale. If sieved through a sieve of  $\frac{1}{2}$  inch wire mesh, the manure gets a fine polished appearance and is free from stones, glass pieces, etc.

During summer, plenty of moisture is necessary for the fermentation and disintegration of the stuff. During the hot season, therefore, water will have to be sprinkled thrice daily on the heaps. This will not be found necessary in winter. A uniform temperature of  $120^{\circ}\text{F.}$  to  $150^{\circ}\text{F.}$  should be maintained. Use a thermometer and if the temperature falls low, sprinkle water and set the heaps. In the winter season, cover the heaps with *cadjan* leaves to keep the temperature uniform.

A hardened ground of 300 feet by 200 feet is all that is required to conduct this operation for a municipality such as Trichur. Proper cross-roads for the transit of vehicles carrying night-soil and rubbish have to be provided on the ground.

The site for the manufacturing of manure by this method should be selected at least 2 furlongs away from the outskirts of the town, though the site can be situated nearer the town, if the manufacture of manure is done throughout under expert supervision. The wind factor should also be taken into consideration in selecting the site. It is inadvisable to select a site more than 2 furlongs away, as it would make the transport of rubbish and night-soil to the place of operation difficult and costly.

The following data showing the working of the process in Trichur town will give an idea of the working cost. About 6 to 6½ tons of night-soil and 8 tons of rubbish are collected daily in this town, with a population of 57,500. The usual basis of calculations is about ½ lb. of night-soil per head per day and ¾ lb. of refuse per head per day of population. But all the night-soil in the town is not collected, as some houses use septic tanks and other types of latrines. Seven rubbish heaps of 300 feet long and 5 feet wide at the bottom are prepared. Apply night-soil emulsion on the first heap on the first day and on the second heap on the second day and so on for 7 days, and raking every third day. Repeat weekly one application on a heap for 7 weeks. For the conversion of the above quantity of night-soil into manure, 10 scavengers are employed, and their work distributed as follows:—

Two scavengers for sorting rubbish, 2 for forming heaps, 2 for raking up heaps and making up the heaps fit for trenching next day, 2 for making trenches in the raked heaps for night-soil application and covering the trenches, 2 for pumping and storing water, spraying water on the heaps, etc. etc. The annual pay of

scavengers at Rs. 14 per mensem comes to Rs. 1,480; one mistry at Rs. 25 per mensem comes to Rs. 300. Recurring charges such as implements, etc., Rs. 120.

There is an output of 1,000 to 1,200 tons per year, and if sold at Rs. 4 per ton it will fetch Rs. 4,000 to Rs. 4,800. (Recently the municipality reduced the cost of manure to Rs. 2 per ton to encourage the agriculturists in the 'grow more food' campaign. This cannot however be taken as permanent cost. It can reasonably be increased to Rs. 5.) Thus the working cost comes to Rs. 1,900 and the sale proceeds come to Rs. 4,000 to Rs. 4,800, if sold at Rs. 4 per ton thereby making a profit of Rs. 2,100 to Rs. 2,900 per year.

The tools, etc., required for the process are:—

- |                    |                     |
|--------------------|---------------------|
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Potassium	..	..	0.181
Phosphorus	..	..	1.002
Calcium	..	..	0.756

These principles are therefore found to be more in the compost manure than in farm-yard manure.

## Current Topics

### Economy of Dressings

By H. RATHLE

CAPTAIN, R.A.M.C.

(From the *Journal of the Royal Army Medical Corps*, Vol. LXXXI, October 1943, p. 190)

THE experience resulting from about 4,500 cases amongst native labourers in six months enables me to recommend this formula for an ointment for treatment of infected wounds, cuts and tropical ulcers.

#### Formula

Cod-liver oil	..	..	40 parts
Oxide of zinc ointment	..	..	60 parts
Copper sulphate powder	..	..	1 part

The cod-liver oil and oxide of zinc alone would have permitted the continuance of infection. The copper sulphate, in this form, is very effective. The whole preparation is very cheap to produce.

In fact, those wounds and ulcers which would have taken weeks for recovery with, on the whole, bad cicatrices, were cured completely within a few days with, in addition, the following advantages:—

(a) Disappearance of pus after twenty-four hours,

(b) disappearance of burning sensation, and (c) rapid appearance of red granulations in the centre of the wound and spread of cicatrization at its edges.

The dressings are changed almost every day for the first two or three days but, later, can be left on the wound for four or five consecutive days. In addition, the patient can carry on with his ordinary duties and, when changed, the dressing, not being sticky, does not hurt either the patient or the processes of healing.

One of the principal advantages is the great economy in dressings which is about 70 per cent.

This formula can be made use of even on wounds of moderate size.

Applied by me on about 4,500 cases of accidents at work, it has always given surprising results.

### Classification Points in Anæmia

(From the *Lancet*, ii, 6th November, 1943, p. 576)

ONLY a few years ago the size of the red blood cells and the colour index were the criteria for classification of anæmias. Since then work on normal and pathological erythropoiesis, and the corresponding observed changes in red-cell size and shape, have shown that these classifications were only partially correct and



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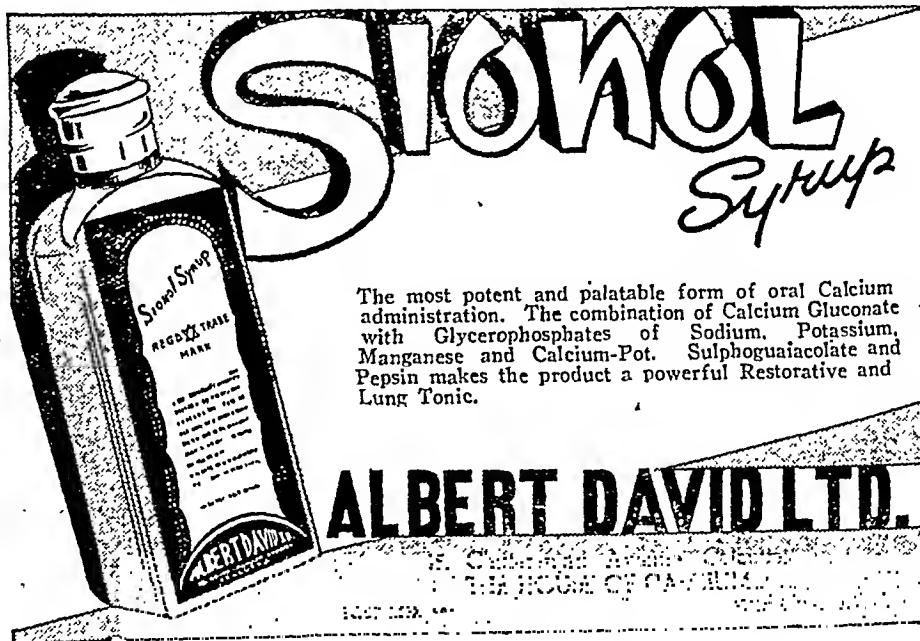
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often positively misleading. The current British view is that stated by Israels in 1941: it recognizes two types of erythropoiesis, normoblastic and megaloblastic; in post-fœtal life, at any rate, the latter is always pathological; megaloblastic erythropoiesis is nearly always associated with increased average cell size and increased mean cell volume; in normoblastic erythropoiesis the average size of the cells may be normal, decreased or increased in different types of anæmia. Israels held that the two types of erythropoiesis are not interchangeable, and Jones reaches the same conclusions in a recent American review. Jones pleads for eradication of the ideas on erythropoiesis dating from Doan and Sabin's work on non-pathological material in 1925—ideas that have only lately disappeared from British textbooks and are still repeated in most American ones. He points out that megaloblasts are found 'almost entirely, if not exclusively, in patients with macrocytic anæmias of the type due to a deficiency of liver principle', and he confirms the observation that large-cell anæmias are often associated with normoblastic erythropoiesis, which means that cell size does not by itself indicate what sort of anæmia is present and what treatment is appropriate.

Another valuable help in classification is Wintrobe's finding that red cells never seem to be over-filled with hæmoglobin. They may be normally or less than normally filled: this is estimated by measuring the mean corpuscular hæmoglobin concentration, which is the ratio of the hæmoglobin content of the blood (grammes per 100 c.cm.) to the volume of the packed red cells (hæmatocrit). Thus for the morphological characterization of an anæmia we nowadays want to know these three things:

1. Is erythropoiesis normoblastic or megaloblastic, and if it is normoblastic what qualitative variations are there in activity and morphology?

2. Is the mean cell volume (MCV = ratio of hæmatocrit to red cell count) normal (normocytic), or larger (macrocytic) or smaller (microcytic) than normal?

3. Is the mean corpuscular hæmoglobin concentration (MCHC) normal (normochromic) or less than normal (hypochromic)?

In pernicious anæmia there is megaloblastic erythropoiesis with a high MCV and normal MCHC; the common iron deficiency anæmia shows a distorted normoblastic erythropoiesis with low MCV and low MCHC; a hæmolytic anæmia may show hyperplastic normoblastic erythropoiesis with high MCV and normal MCHC. In temperate climates this morphological characterization of an anæmia corresponds, for the most part, to well-defined clinical entities; so if we find a macrocytic normochromic megaloblastic anæmia we are justified in diagnosing one of the pernicious group of anæmias and proceeding with the clinical and laboratory investigations that will identify it. In temperate climates too, megaloblastosis is always associated with macrocytosis and macrocytic anæmia, whether megaloblastic or normoblastic, is always normochromic. But in tropical anæmias it seems that almost any combination can be found; Trowell reported macrocytic hypochromic anæmia with or without megaloblastosis of the marrow in Uganda, and in our 23rd October issue Foy and Kondi reported the extraordinary combination of megaloblastic marrow with a microcytic normochromic blood picture. These bizarre findings, however, in no way invalidate the fundamental conclusions about the classification of anæmias; they occur in patients suffering from multiple deficiencies, often over long periods, so that the morphological characterization of the anæmia—reached by determining *average* results—only expresses which of the various deficiencies has, at the time of the examination, gained the upper hand.

As Foy and Kondi emphasize, it is especially important in deficiency anæmias to study the qualitative changes in the blood and bone marrow and to relate these to all the available clinical information before making a diagnosis. Correct classification depends not only on accurate estimation of the hæmatocrit and the usual blood figures, but also on what

Jones calls the 'disciplined' eye' and 'the ability to recognize and appreciate differences in nuclear structure, the ability to separate pathologic from normal cells and the ability to separate normal or hyperplastic marrow patterns from dysplastic ones'. Unfortunately facility in these distinctions is not easily acquired and needs experience, but, as this newer knowledge becomes disseminated, experienced investigators are able to report comparable studies. These studies on tropical nutritional anæmias may give us new information about the factors that influence blood formation, and at this time they have more than a theoretical interest, since it is only too likely that nutritional anæmia will be one of the problems that we shall have to deal with soon in Europe.

## A Simple Field Test to Detect Quinine in Urine

By COLONEL V. H. CORNELL

and

CAPTAIN S. KAYE

(From the *Military Surgeon*, Vol. XCIII, August 1943, p. 133)

A NEW reagent is described which has been found to be markedly sensitive in the detection of quinine. The use of this reagent has proven of value as a field test in establishing the presence of minute amounts of quinine directly in urine without prior extraction. Large numbers of men may be checked in a very short time with a minimum of assistance and equipment.

A comparative study was made of the various alkaloidal precipitants which were reactive with quinine; of these it was found that Mayer's reagent and Tanret's reagent were most sensitive.

Our reagent is four times more sensitive than Tanret's reagent and twelve times more sensitive than Mayer's reagent for the detection of quinine in urine, as determined by tests on decreasing concentrations. It is sensitive to one (1) gamma (one-thousandth of a milligram) in 1 ml. of urine.

A five-gram tablet was ingested by each of twelve subjects and the quinine output followed and tested with Tanret's, Mayer's, and Kaye's reagent, every hour.

Reagent	Number of hours positive after ingestion of quinine	
Tanret's	..	30
Mayer's	..	20
Kaye's	..	36

Another series of six subjects was studied, who had taken the full prophylactic dose (45 grains of quinine) over a period of three days. The urine output was positive for quinine in all six cases up to the 46th hour. Thereafter, one after the other showed negative quinine, until the last one also was negative at the fiftieth hour.

A third series of fifty men was studied, twenty-five of whom had not had quinine for at least fifty hours and twenty-five of whom were each given a 5-grain tablet. All twenty-five abstainers proved negative on test. The twenty-five who had taken the quinine were tested two hours after ingestion. Twenty-one showed heavy positive reactions. The four negative were tested each successive hour. One became positive the third hour. The other three showed a positive reaction on the fourth hour. This would indicate that these four men had a slower rate of absorption since all tablets came from the same lot.

The reaction between the reagent and quinine is rapid, forming an immediate turbidity which varies with the concentration of quinine present. In the presence of very minute amounts of quinine, it would be well either to allow the solution to stand awhile after which an intensification may be observed, or to



bring the solution to a slight boil and then observe turbidity on cooling.

The following substances, however, interfere with this reaction: atropine, cocaine, strychnine, albumin, and atabrine. The alkaloids would be uncommon and unlikely to be found in tests of field troops. Albumin may be more frequently encountered and its presence may give false positives. In a suspected false positive, a simple differentiation may be made by heating the tube with a portable alcohol lamp. The quinine precipitate will dissolve when heated and reappear when cooled. The albumin precipitate will intensify when heated and persist. The few cases with albumin will not interfere when large groups are checked where the majority are either positive or negative. Since atabrine and quinine are both anti-malarial agents and the purpose of this field test is to recognize the presence or absence of such reagents, there is no need for differentiating between them. However, the sensitivity of this reagent is not sufficiently great so as to identify small amounts of atabrine present in urine. The sensitivity for atabrine in urine is 25 gamma per ml. of urine.

#### PREPARATION OF REAGENT

3.0 gm. red mercuric iodide.

2.0 gm. potassium iodide.

20.0 ml. glacial acetic acid.

Distilled water, sufficient to make 60 ml.

These chemicals may be mixed in any order and are shaken or stirred into complete solution. This reagent is quite stable but should be kept in a brown bottle.

#### PROCEDURE

In field tests we have examined men in groups to correspond with the number of tubes in the rack used, giving them serial numbers and collecting urine simultaneously from all in small wide-mouthed bottles. Approximately one (1) to two (2) ml. of urine is used for a test. To this is added five (5) to ten (10) drops of our reagent. An immediate turbidity which appears on slight agitation is an indication of quinine. This will intensify on standing.

#### SUMMARY

1. A procedure is described for the detection of quinine in urine, using a new and very sensitive reagent.

2. This test is both rapid and simple, using a minimum of equipment and may be used to check large numbers of troops in the field.

### Bone Marrow as a Site for the Reception of Infusions, Transfusion and Anæsthetic Agents

By H. BAILEY, F.R.C.S.

(From the *British Medical Journal*, i, 5th February, 1944, p. 181)

As my experience in several surgical centres separated by some distance is precisely the same, I have assumed—I think correctly—that it represents a cross-section of the present attitude of the profession towards bone marrow as a site for infusion and transfusion: there are but few who have used this route a dozen times, and many are apprehensive about introducing a cannula into the sternum.

It is preferable that I should be less inclined to voice an opinion on a comparatively new procedure were it not for past memories. Ten years ago, when I pressed for the more general adoption of *continuous* intravenous saline (Bailey and Carnow, 1934), I met with initial reluctance, if not active opposition, towards the (then) unfamiliar procedure. At that time, although I had divided my previous ten years among surgical posts in three university cities and one London teaching hospital, I had never seen a *drip* infusion or transfusion performed. To-day there is no difficulty in getting continuous intravenous fluid therapy carried out.

On the contrary, one has to exercise constant vigilance in curtailing its use; for as sometimes happens, enthusiasm, particularly enthusiasm unyoked to physiological understanding, leads to the abuse of good remedies.

It was from the American and Canadian literature that my interest in continuous intravenous saline infusions was stimulated. So with bone marrow as a receptor; I had never even thought of a medullary cavity in connection with the reception of parenteral fluid until I read the paper by L. M. Tocantins and J. F. O'Neill (1941).

At first I employed bone puncture as a last resort, for instance, in those occasional cases in which most of the available veins had been utilized previously. As time went on I found an increasing field of usefulness for marrow infusion, and now I am prepared to state that the medullary cavity of the manubrium is as good a receptor as a vein for infusions of all kinds and for pentothal anæsthesia. In a few instances I consider bone marrow is a better avenue for infusion than a vein, and to bring this belief to the notice of those who may be called upon to resuscitate the very shocked and the very young is the main object of this communication.

#### ADVANTAGES

1. In very shocked patients there is difficulty, sometimes considerable difficulty, in cannulizing a vein. Even when the cannula is *in situ* the veins may be so collapsed that the reception of parenteral fluid is unsatisfactory, and one must stay with the patient and employ various devices to expedite the flow. Sternal puncture is a more crude procedure which is effected mostly by 'feel'. Once entry to the medullary cavity has been gained, the flow of fluid into the marrow is unaffected by those factors which militate against unhampered intravenous fluid therapy.

2. Sternal puncture can be carried out in a comparatively poor light—a most important consideration under black-out conditions, with experience and good organization, it should be possible for a medical officer to cannulize the sternum and start infusions more rapidly and more certainly than he could hope to do when cannulizing veins under similar circumstances.

3. Those who have had to give intravenous infusions to dehydrated infants will welcome the tremendous advantages of bone marrow as a receptor. It is certain; it is safe—at least I have neither seen nor heard of any ill effects from inserting a Witts sternal-puncture needle into the tibia and gravitating saline, glucose, or plasma into the bone marrow. At any rate, I am sure that I am correct in stating that this procedure is safer than utilizing the superior longitudinal sinus.

4. A cannula in the sternum is 'out of the way' when an operation is being performed on the abdomen or lower extremity. In such circumstances, the whole of the infusion paraphernalia being near the head of the patient, it is convenient for the anæsthetist to attend to the infusion without moving from his accustomed position.

5. Thrombosis and phlebitis, of course, cannot occur. These inseparable complications of intravenous fluid therapy are admittedly infrequent: with correct technique they should not exceed 1 per cent, but my impression is that this incidence is exceeded.

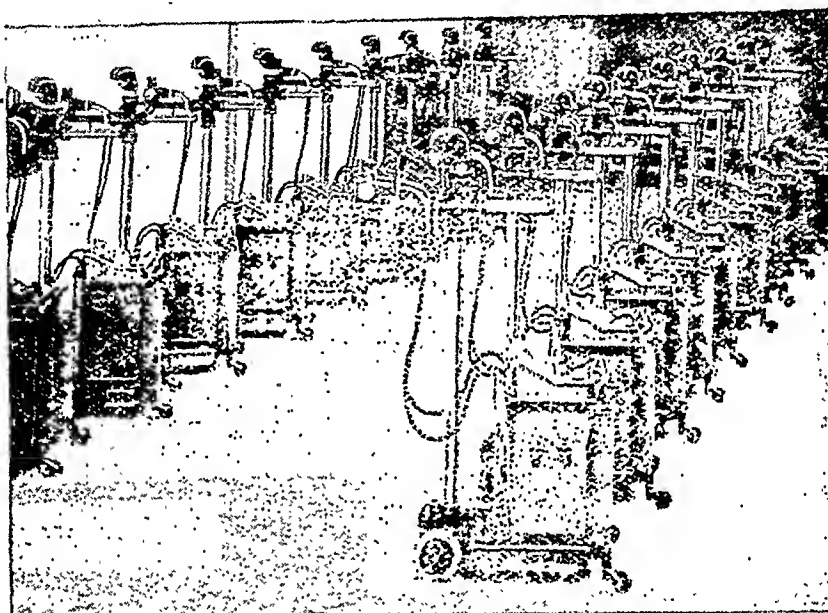
#### DISADVANTAGES AND DANGERS

1. Theoretically, osteomyelitis may result. In an experience of over 60 cases I have seen no sign of it.

2. Whole blood cannot be introduced as rapidly as into a vein by gravity. The apparatus designed by Messrs. Evans Sons Lescher and Webb overcomes this difficulty, for introduction is speeded up by oxygen pressure. Raising the intramedullary pressure is inclined to give pain.

3. The only real danger is that both plates of the manubrium may be perforated and the fluid be introduced into the superior mediastinum. This is not a theoretical conception, for it occurred in my practice when performed by an extremely capable house surgeon. It is desirable to add that in this instance an

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0.15 gm.	0.75 gm.
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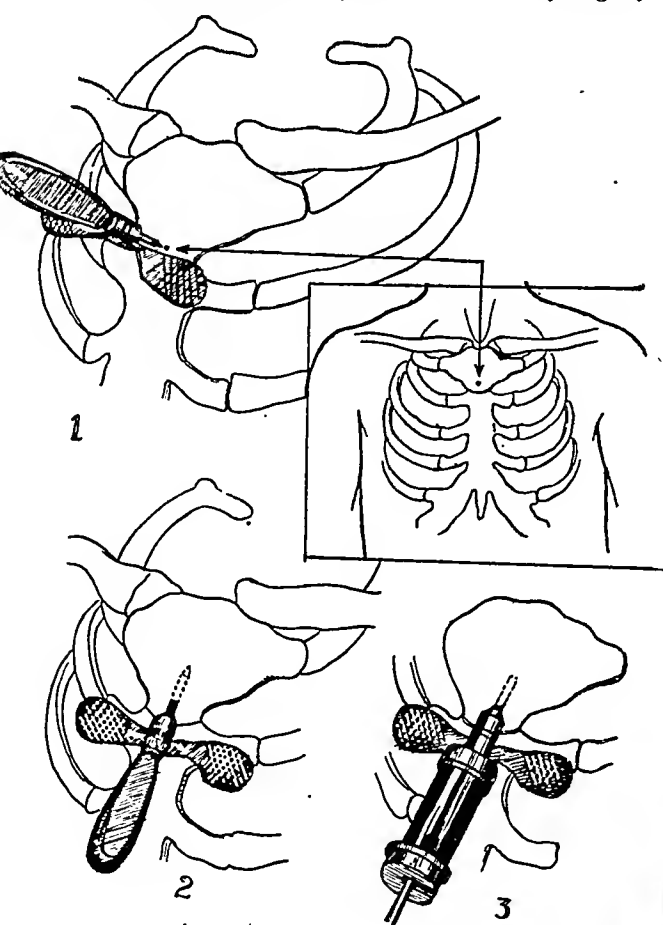
'unwinged' Wits needle was employed and, fortunately from our point of view, the patient was suffering from hopeless malignant disease. The cannula shown in the accompanying illustrations can be regarded as fool-proof provided the simple technical details given below are followed.

#### TECHNIQUE

The patient lies prone. A wheal of local anaesthetic is raised on the skin in the middle line just above the manubriogladiolar junction. Using a large but short hollow needle, the point is driven right on to the bone and about 2 c.cm. of 1 per cent solution of novocain is infiltrated. This subperiosteal infiltration is an important detail. The area is then massaged with a swab so as to disperse the anaesthetic and enable one to feel the manubriogladiolar synchondrosis.

The trocar and cannula is inserted just above this ridge (figure 1) and pointed almost directly downwards towards the floor, but with a very slight inclination towards the patient's head. An unhurried boring motion is imparted to the instrument. The pressure, at first slight, is increased. The feeling that the outer plate has been penetrated is unmistakable. Penetration being accomplished, the angle of the instrument is altered and the point is directed towards the patient's head. The wings do the rest—they ensure that the correct depth has been reached, they set the correct angle, and they prevent too deep penetration (figure 2). The trocar is removed. The next step is to take a 10- to 20-c.cm. record syringe half full of sodium citrate solution, which is in readiness. The syringe is affixed to the cannula and some of the citrate solution is injected. The piston is withdrawn. If what appears to be blood (it is red marrow) is easily and liberally withdrawn so that it colours the whole of the contents of the syringe (figure 3) the extremity of the cannula is correctly placed within the marrow cavity. If the flow of marrow is not entirely free, the trocar is reinserted into the cannula, which is then very slightly

withdrawn and another attempt to aspirate marrow is made. When entry of the tip of the cannula into the marrow cavity is undeniable, more citrate is



Figs. 1, 2 and 3.

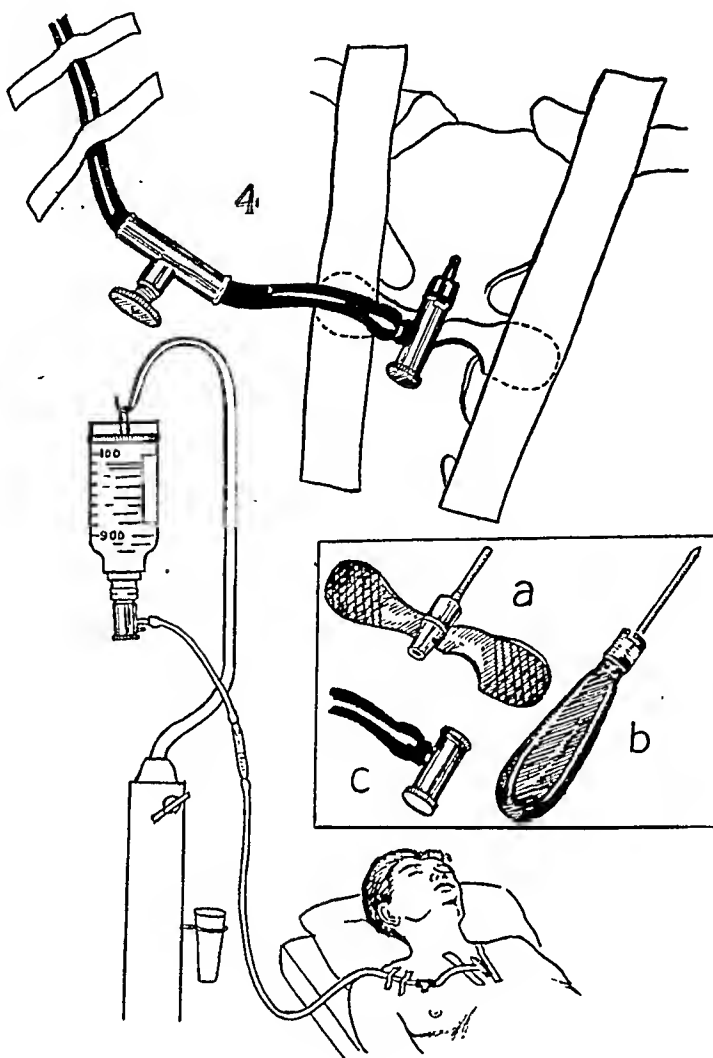


Fig. 4.

injected and the syringe is disconnected. Quickly the cannula is linked with the infusion or transfusion unit, the tubing of which has been previously demonstrated to be free from air bubbles. Strips of adhesive plaster of an appropriate width are used to fix the wings to the chest wall, and narrow strips of the same material are placed to steady the attached tubing at the correct angle (figure 4).

Spectators unfamiliar with the method invariably remark (a) how painless is the procedure; (b) how easily fluids gravitate into the medulla—they liken the rate of gravitation (before it has been damped down) to that expected after entry of a large unobstructed vein.

For want of ocular demonstration, generations of surgeons have suspected that too often broken bones are filled not with red marrow but with black ingratitide. It may well be that the rising generation will verify almost daily that even in old age the normal sternum is full of marrow so red and so fluid that on macroscopic acquaintance it is indistinguishable from freshly drawn blood.

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## Plasma in Plenty

(From the *Lancet*, i, 3rd June, 1944, p. 730)

TECHNICAL advances, greater knowledge and generous facilities have combined to increase the demands for blood and blood substitutes. A modern general hospital of 1,000 beds can be expected to use anything up to 1,000 pints of blood and plasma in a year for medical ailments, maternity work and accident cases. This will need a service collecting between 2,000 and 3,000 pints of blood in a year, if the stable blood substitutes—plasma or perhaps albumin—are to be available for accidents and emergencies. So far the only source of plasma has been the ordinary blood donor, who, on conservative grounds, is not bled more often than once in three months, and in whom blood regeneration has to be considered or even assisted. No one anticipates that the war panel of patriotic donors can be maintained at its present numbers indefinitely, so any device for lightening their load or transferring it to another source can be counted an advantage. There has always been an Anglo-Saxon prejudice against the use of cadaver blood—a prejudice which the Russians dismissed, though later they found themselves in technical difficulties when using blood itself. Yet Erf has shown that there are no technical difficulties in the preparation of dried plasma from this source, and that the product is the equal of that supplied by the living. Human albumin, which war may show to be as good as plasma, can be obtained in the same way, and here there is no objection to removing as much as can be collected. More attractive perhaps is the technique described by Co Tui, Bartter, Wright and Holt, who advocate the bleeding of donors for plasma alone. After separation of the plasma, the red cells are reinfused. Working under these conditions donors can give as many as four donations in a week or one donation every week for twelve weeks without any effect on their plasma protein, haematocrit, bilirubin level or fragility test. Such methods may have to be applied to keep up the supply until plasma or albumin of animal origin has been rendered safe for human use.

## Microbiologic Analysis of Vitamins

(From the *Journal of the American Medical Association*, Vol. CXXIV, 26th February, 1944, p. 578)

ALMOST a century ago micro-organisms were recognized as sources of danger to man in the fields of medicine, of technology and of food preparation. However, conviction has also prevailed that certain bacteria, molds and yeasts are also of great service to mankind. The fermentation industries, including distilling, brewing and baking, the production of organic foods, acid on a commercial scale, the cheese industry, the white lead industry and recently the production of penicillin are among the many commercial activities based on one or more phases of the peculiar metabolism of micro-organisms.

Recently yeasts, molds and bacteria have been found extremely specific in their nutritive requirements; in many instances these micro-organisms need the food factors which have been shown to be important in promoting the nutritive success of mammals. By suitable adjustment of the basal medium the amounts of vitamins present in a sample may be determined by measuring the growth of the micro-organism or the formation of some product of its metabolism under narrowly controlled experimental conditions. As a result the time-consuming bioassay for vitamins with laboratory animals and the laborious chemical methods have been supplemented, and to some degree replaced, by the more rapid microbiologic assays, particularly in connection with estimations of the vitamins in the B complex. Thus various strains of yeast have been employed for the quantitative determination of thiamine (B<sub>1</sub>), pyridoxine (B<sub>6</sub>), biotin and inositol; either the production of carbon dioxide or the turbidity caused by the growing yeast cells

serves as a criterion of response. *Lactobacillus casei* B<sub>7</sub> requires riboflavin, biotin and pantothenic acid for growth, and the titration of the lactic acid produced by this organism during a period of incubation serves admirably as a quantitative measure of these vitamins in the medium. At present the estimation of the concentration of niacin in a sample is made by employing *Lactobacillus arabinosus*. A mold, *Neurospora sitophila*, is used to measure the amount of pyridoxine (B<sub>6</sub>) in food materials and tissues; in this case the final estimation is made by weighing the dried mycelium.

The foregoing are representative examples of microbiologic vitamin analysis. The accepted methods of this class give results agreeing satisfactorily with chemical and animal assays. Economy of time and space represent the great advantages inherent in microbiologic assays. Further studies of the metabolic needs of micro-organisms will indicate further use for yeasts, molds and bacteria in biochemical analysis, with consequent immediate benefit in food analysis and ultimate advantage in medicine.

## Effects on Rats of Prolonged Feeding with the Staple African Diet

By J. GILLMAN, D.Sc., M.B.

(From the *British Medical Journal*, i, 29th January, 1944, p. 149)

It is known from numerous surveys and observations that pulmonary tuberculosis and other diseases of the respiratory tract are especially prevalent among the Africans (South African negroes). It is also common knowledge that cirrhosis of the liver and especially primary cancer of the liver are very often encountered in this people. In an extensive investigation into the incidence of cancer in South Africa, Berman has shown that in a series of 253 cases of cancer of all organs in adult male Africans working in the Witwatersrand gold mines no fewer than 222, or 90 per cent, were primary in the liver. This remarkable state of affairs is even more strongly emphasized when it is remembered that liver cancer is the rarest neoplasm in Europeans.

Several factors are regarded as contributory to this high incidence of cancer, one of which is cirrhosis, which is almost invariably associated with liver cancer. There is a considerable body of opinion which regards this susceptibility to liver cancer in the pigmented peoples as due to some racial factor. Des Ligneris has shown that extracts from the cancerous and non-cancerous livers of Africans are capable of producing neoplasms of the skin when painted on the backs of mice. The extracts from the normal Europeans are said to be less potent in this respect. A similar experience has been reported by Hieger.

### EFFECT OF AFRICAN DIET ON RATS

Malnutrition among the Africans is widespread in South Africa. The overwhelming majority fed on a diet consisting largely of maize meal (mealie pap) and sour milk. This forms the staple from the time of weaning throughout life. Before invoking a racial or a genetic factor in modifying the incidence of disease it seemed highly desirable to ascertain the effect of the African diet on normal animals. Accordingly 125 rats weighing from 45 to 50 g. were fed exclusively on mealie-meal porridge and sour milk. The mealie-meal porridge was concentrated to form a solid mass, while the sour milk was prepared from fresh milk allowed to ferment in a warm room. The animals received liberal amounts of this food. Apart from thinning of the hair over the abdomen and hind legs and roughening of the tail, no obvious signs of acute avitaminosis were recognized.

After 14 months 12 rats were killed and a full post-mortem examination was performed. The others are being studied biochemically. In all of those killed

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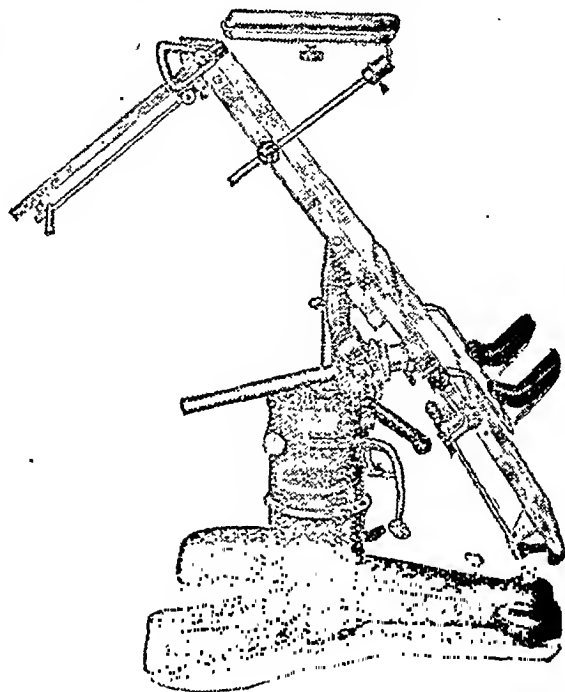
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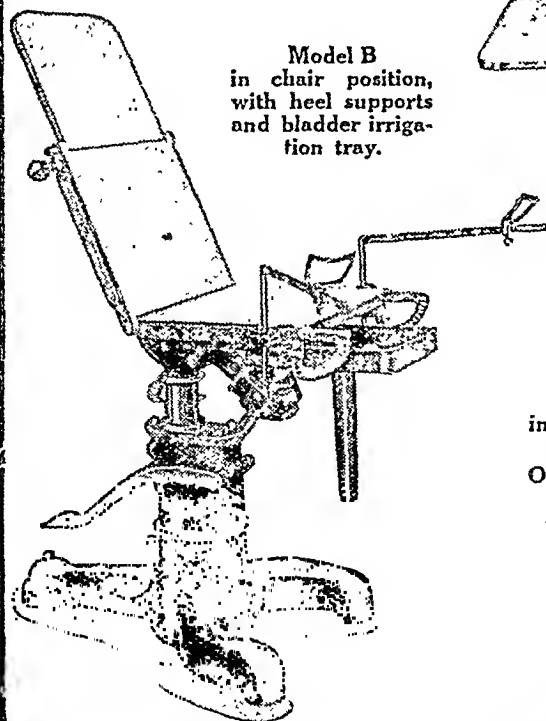
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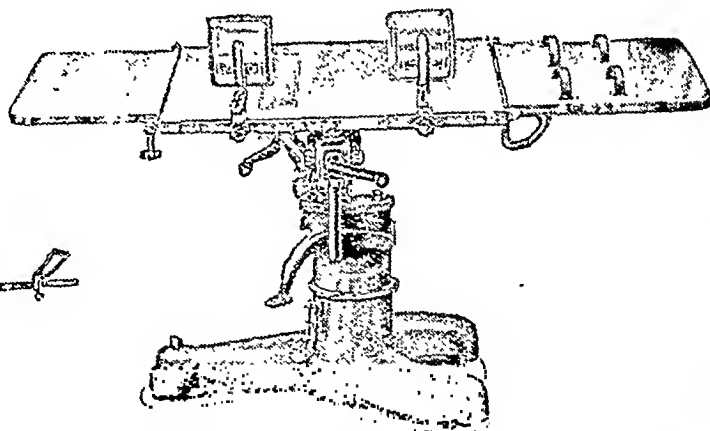
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some degree of liver pathology was evident macroscopically. This varied from diffuse enlargement of the whole liver with obvious fatty change to a widespread nodular cirrhosis, the latter usually involving the left side of the liver. In one case there was complete atrophy of the left lobe with enormous compensatory hypertrophy of the right lobe—so much so that the enlarged lobe extended almost into the pelvis. In this instance the remains of the left lobe could be seen as two small appendages of cirrhotic tissue.

In this series of rats it seemed that the liver first enlarged and underwent fatty changes and later cirrhosis supervened, or else complete atrophy of the affected lobes occurred, with corresponding enlargement of the right side. The heart was grossly enlarged, and in nine cases one or both lungs showed recent or old-standing inflammatory lesion with areas of bronchiectasis or abscess formation. The fat in the mesentery, retro-peritoneal, or subcutaneous regions was abundant. The skull was very much thickened, especially in the occipital region. The suture lines could be readily identified by the zones of great vascularity. The upper incisor teeth were particularly affected; many of them were broken, some fused, and others loose. The pituitary was enlarged, the thyroids were atrophied, and the suprarenals were small and of greyish colour. In four cases the lymph glands of the peri-oesophageal region and above the lesser curvature of the stomach or above the abdominal aorta were of dark-brown colour, due to the presence of hæmosiderin. The jejunum in those cases of advanced cirrhosis contained a dark viscid material which gave the reaction of blood. It is noteworthy that although many thousands of rats were examined post mortem over a number of years no lesions in the liver of the kind described above were ever observed.

#### COMMENT

The significant features of this feeding experiment in rats are the gross pathology in the liver, the frequency of lung lesions, the enlarged heart, the abundance of adipose tissue, the thickened skull, and the dental affections, all of which occurred without any recognizable manifestations of acute vitamin deficiency. The production of liver damage by means of a diet which forms the staple of the overwhelming number of Africans in South Africa is not without its sociological implications. It may also have repercussions in other parts of the world where economically impoverished individuals are forced to live on a diet similar to that of the African in the Union of South Africa.

### Combined Penicillin and Heparin Therapy of Subacute Bacterial Endocarditis

By L. LOEWE, M.D.  
P. ROSENBLATT, M.D.  
H. J. GREENE, M.D.  
and  
M. RUSSELL

(Abstracted from the *Journal of the American Medical Association*, Vol. CXXIV, 15th January, 1944, p. 144)

1. SEVEN consecutive patients with subacute bacterial endocarditis have been treated by a method which combines the uses of penicillin and heparin. Further observation will be required to determine the permanence of results, but the immediate effects suggest uniformly successful sterilization of the blood and relief of clinical manifestations.

2. Penicillin has been given in requisite dosage by the method of the continuous intravenous drip. One patient, however, also received the drug intramuscularly.

3. Heparin has been deposited subcutaneously in most instances but was occasionally given in the intravenous infusion.

4. There has been no significant toxicity as the direct result of therapy. In point of fact, treatment was well tolerated and each of the patients exhibited

striking well-being during and after the active period of treatment.

5. In a few of the patients the efficacy of the therapy may have been enhanced by the preliminary use of sulphonamide.

6. Post-therapy management included the removal of possible foci in the teeth and nasopharynx. These surgical procedures were accompanied by additional prophylactic chemotherapy with penicillin.

### Dietary Injury of the Liver

(From the *British Medical Journal*, i, 12th February, 1944, p. 229)

(A letter from H. P. Himsworth and L. E. Glynn)

We have read with interest in your issue of 29th January the article by Dr. Joseph Gillman entitled 'Effects on Rats of Prolonged Feeding with the Staple African Diet'. Dr. Gillman reports that rats given a diet of maize meal and sour milk develop a 'nodular cirrhosis' of the liver, which usually involves the left lobes of the organ. We have produced a similar lesion by means of diet. The lesion in question however, is not a cirrhosis in the strict sense of portal cirrhosis; it is the condition of nodular hyperplasia, and it is the sequel to massive hepatic necrosis. In our animals we have produced every stage of the lesion from acute yellow atrophy through post-necrotic scarring to nodular hyperplasia. We have been able to show that this massive hepatic necrosis, with its sequel of nodular hyperplasia, is a deficiency disease due to lack of a constituent of protein, and that according to the degree of deficiency the condition involves the whole organ or only the left lobes. The experimental results giving the proof of this statement are now in the press and will be published shortly.

### Congenital Malaria

(From the *Lancet*, i, 29th January, 1944, p. 156)

For many years the weight of evidence seemed to be against transmission of malaria through the placenta; but well authenticated examples of such transmission have steadily grown in number. Among the more striking cases reported is that of Jones and Brown in which a woman returning from a holiday on the continent had several bouts of malaria during her pregnancy and was delivered in Buckinghamshire (where there is no indigenous malaria and anopheles are not usually found) of a child who developed malaria 16 days after birth, the organism being *Plasmodium vivax*. Hale, Tanner and Hewlett reported congenital malaria in one of a pair of twins, born in London in January—which made transmission by mosquito exceedingly unlikely. *P. vivax* was again the invader. Buckingham has demonstrated *P. falciparum* in the blood of a foetus before birth. Blacklock and Gordon in Sierra Leone found that in 38 per cent of pregnant women infected with *P. falciparum* the maternal villi of the placenta became intensively infected, and the foetus died though no parasites were found on the foetal side of the syncytio-trophoblast layer. Jean and Van Nitsen found malarial schizonts in the spleen of 8 children of malarial mothers, born dead, or dying shortly after birth. Wickramasuriya describes 6 cases in which malarial parasites were found in the placenta and also in the blood of tissues of the infant, either before or just after birth; he considers that transmission of the infection may often cause death of the foetus: only one of the 6 infants survived. Lately Cohen, working in a malarial district of Latin America, has published 6 more cases in which the mother was infected and parasites were present in the peripheral blood of the child at birth. He has also noted 3 cases of 'latent malaria' in babies born of women with chronic malaria. No parasites were found in the blood of these infants, but they failed to thrive and lost weight until given 'equinine' after which they grew up normally. As a result of this study, Cohen gives equinine to malarial women during pregnancy in doses not exceeding 0.9 gramme daily,

and finds there is no added tendency to abortion—indeed, the drug may prevent it.

The mechanism of transmission is still not clear. Wickramasuriya was struck by the unusually dark and friable placentas of some of his malarial cases and this led him to investigate the possibility of trans-placental fetal infection. He found that parasites become aggregated in the placenta, and it is possible in some cases to find positive placental smears where blood examination has been repeatedly negative. It is usually assumed that an intact and physiologically healthy placenta will not permit the passage of parasites, and some mechanical breach is therefore usually postulated. Lopatin suggests that the child may be infected at parturition during detachment of the placenta, when maternal and fetal blood may mingle. This would not account, however, for cases of intra-uterine infection; and it may be supposed that the pathological changes induced in the placenta by malaria are sufficient to make it permeable by the parasites. This seems to be borne out by Wickramasuriya's finding that transplacental infection is most commonly by the malignant tertian parasite—the most destructive of the plasmodia.

## Reviews

**KNOWLES'S INTRODUCTION TO MEDICAL PROTO-ZOOLOGY.** Second Edition. Revised and abridged by B. M. Das Gupta. 1944. U. N. Dhur and Sons, Limited, Calcutta. Pp. xviii plus 323, with 104 illustrations and 10 coloured plates. Price, Rs. 20

This work is a greatly abridged edition of Knowles's 'Introduction to Medical Protozoology', and is primarily intended for the use of students at the Calcutta School of Tropical Medicine. Such abridgements of textbooks are notoriously difficult of achievement if only the useful is to be retained and all the redundant omitted, and if the resultant offspring of the parent book is to remain a well-balanced and symmetrical work.

It may be said, at once, that with only one reservation mentioned below, the present editor has succeeded admirably in this task, and that the new matter which he has incorporated has been skilfully introduced without interfering with the general balance of the original work. The main arrangement of the original book has been adhered to, so far as the abridgment allows, and this is excellent.

Before making the few comments which space allows on the treatment of the various groups of protozoa, the reviewer wonders why, in omitting the redundant matter, the editor has retained the section on spirochaetes in an abridged textbook on medical protozoology when he himself remarks in chapter I that 'they are certainly not protozoa'!

Considering the fact that they are, at best, 'gate crashers' in a textbook on protozoology surely 28 pages is too generous an allowance when not more than 43 are accorded to the *Plasmodia*, animal as well as human.

It is a pity that the first genus of parasitic amoebæ dealt with should be miss-spelt as '*Endambæa*' on p. 15 as the heavy type brings the mistake into prominence. The account of the parasitic amoebæ is clear and concise, and the table of differential characters appended will be welcomed by the student.

In the chapter on Mastigophora there is an omission in the section on the genus *Bodo*. While the record of Powell and Kohiyar (1919) of a bodo-like organism in the urine is mentioned, the earlier record by Sinton (1912), and even earlier records, is omitted.

Another defect in the alignment of letters occurs in the spelling of the order *Diplomonadida*, and these errors in bold type are especially regrettable as the fault does not lie with the editor. The description of the various genera and species is adequate, and there is, again, a useful table of differential characters.

In chapter IV an excellent account of the genus

*Leishmania* is given, although there are certain omissions. Thus, in the section on the pathology of kala-azar, mention of the faeces as one of the avenues of escape of the parasite from the body of the host is omitted. Again, in the section on susceptibility of animals to inoculation, while some of the animals so susceptible are mentioned, no indication is given of the method of inoculation nor of the form of the parasite to be inoculated. It is important enough to need mention that both the flagellate and Leishman-Donovan body forms of the parasite are infective by inoculation into the tissues, and that both forms as well as flagellates in actual sandflies can also infect when given orally, while the Leishman-Donovan bodies may even infect if placed on the uninjured conjunctive.

In the records of the localities where natural infection with *Leishmania tropica* has been found in animals, a record from the Punjab by Sinton (1938) of infection in a dog has been omitted, although, being an Indian record, it is of interest to Indian students.

In the section on *Leishmania* in animals, mention is made of *Leptomonas* forms obtained in cultures from the blood of the Indian gecko *H. pleadovii*. This reference would have been completed by mention of the record by Shortt and Swaminath (1928) of the finding of typical Leishman-Donovan body forms, presumably of this parasite, in the peripheral blood of Indian geckos in Assam.

In the description of the development of trypanosomes in *Glossina*, no mention has been made of the relationship of the developing trypanosomes to the peritrophic membrane, and of the method of their entry into and exit from the space between this membrane and the gut wall proper. This omission leaves the account somewhat incomplete.

The description of the *Hemosporidiidae* is naturally devoted chiefly to the genus *Plasmodium*, and the description of the human species is very informative and complete considering the condensation which the limits of space imposed on the editor. This is a wholly admirable chapter, every page of which the student should study carefully. Nothing more need be said.

The undue prominence given to spirochaetes in a textbook of protozoology has already been commented upon. Chapters XIV to XIX on laboratory technique are a very useful part of the book, and a good selection of methods has been made. If the student uses these only, he will be well served. Two points may, however, be remarked on. In the section on examination of stools for intestinal protozoa, no mention is made of the very useful method in which a watery solution of eosin is used to stain the fresh preparation. This method not only assists in picking out cysts of amoebæ, but also differentiates dead from living cysts.

The other point for mention is the old, oft repeated, and here italicized warning against using any but violet crystals of iron alum in the iron-haematoxylin staining process. It has been shown that this is by no means necessary, but the 'thirty year' period required to remove a mistake from the textbooks, as mentioned in the preface to the first edition, has not yet expired!

To sum up on this new edition; the reviewer has registered a very pleasing impression of the work as a whole. The format is distinctly good; there are comparatively few printing errors; the type is most pleasing; the illustrations are excellent and well-chosen, and the whole book is a distinct credit both to the editor and to the publishers, as a war-time production.

H. E. S.

[*Note*.—Protozoologists, like the objects of their study, are often invasive, and tend to annex territory which is really outside their province; the standard textbooks usually contain chapters on the spirochaetes and the rickettsiæ.

In including such chapters, the present book is following established precedent; nevertheless it is right that the sins of the protozoologists should be pointed out.—EDITOR, I. M. G.]



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Oct., 1944]

**OUTLINES OF INDUSTRIAL MEDICINE, LEGISLATION, AND HYGIENE.**—By James Burnet, M.A., LL.B. (Lond.), M.D., F.R.C.P.E. 1943. John Wright and Sons Limited, Bristol. Pp. 87. Price, 7s. 6d.

THIS small book is intended for those who are required, or who wish to know something about industrial medicine, legislation and hygiene. Poisons, medical diseases, surgical affections and diseases of the eye and skin are dealt with in the first part of the book; each affection is treated separately with a description of the occupational cause, clinical features and preventive measures. In the second and third parts the author gives the essential portions of the various factory Acts in England, and a brief outline of personal and factory hygiene.

In India industries are rapidly developing, and these no doubt expose workers to some hazards, yet so far as we know there is very little record of any experience with industrial diseases. If this is true, then it is possible that such diseases are being overlooked, as an ordinary medical practitioner cannot claim to have much acquaintance with them. Doctors working in factories will do well to keep a copy of this book in their pocket.

R. N. C.

**BROMPTON HOSPITAL REPORTS: A COLLECTION OF PAPERS RECENTLY PUBLISHED FROM THE HOSPITAL.** Volume XI. 1942. Published by the Research Department of the Hospital. Printed in England by Gale and Polden Limited, Aldershot. Pp. 36. Illustrated. Price, 5s. (Further copies can be obtained from the Secretary, The Hospital for Consumption, Brompton, London, S.W.3. Price, 5s. 7d.; postage free.)

THIS volume contains a series of fourteen articles, all being reprints from medical journals. Maurice Davidson discusses 'modern views on pneumonia and its treatment' and assesses the value of some of the recent methods of specific therapy and refers to the possible disadvantages which they may occasionally entail in comparison with the older methods. Wingfield reviews the modern treatment of pulmonary tuberculosis as it affects the general practitioner. Lewis-Fanning and Maurice Myers examined the blood sedimentation rate in pulmonary tuberculosis, in several hundred patients treated in a sanatorium, from the prognostic point of view, and give results of the investigation. Brooks describes six cases in which a paravertebral abscess resulting from spinal caries ruptured into the pleura or lung and shows that prodromal symptoms suggestive of rupture of the abscess were manifested in each instance and were present for a sufficient length of time to permit of therapy. Case reports are also given of two rare conditions—a right-sided aorta and hydatid disease of the lungs. There are other papers of interest; the last one by Clifford Hoyle deals with 'the care of the dying', a subject of importance but seldom taught by our teachers; students and practitioners will alike benefit from its perusal. As usual with the Brompton reports, there are many illustrations. The book also contains a tribute to the memory of the late Dr. Percy Kidd who was connected with the Brompton Hospital for over sixty years, and who died in January 1942.

R. N. C.

**STUDIES ON IMMUNISATION. FIRST SERIES.**—By Sir Almroth E. Wright, M.D., F.R.S. 1943. (Researches from the Inoculation Department, St. Mary's Hospital, London, W.2.) III. William Heinemann Medical Books, Limited, London. Pp. xi plus 421. Illustrated. Price, 25s.

THIS is the third volume of collected researches from the inoculation department of St. Mary's Hospital, London, and is a reprint, with few changes, of the book published in 1909. It contains a series of studies on

the protective elements of the blood and on vaccine therapy which were published between 1897 and 1908 in scientific and medical journals. The book brings together in one volume papers of historical interest which contributed to our knowledge of immunity in the past. All the authors' ideas, however, are not acceptable at the present day.

R. N. C.

## Abstracts from Reports

### THE ADMINISTRATION REPORT OF THE MEDICAL AND PUBLIC HEALTH DEPARTMENT OF THE NIZAM'S GOVERNMENT FOR 1941-42

#### MEDICAL

THE State has 151 hospitals and dispensaries with 3,084 beds of which 1,384 are for women. During the year 2,940,667 out-patients and 42,277 in-patients were treated; there was some decrease compared with previous years' figures owing to shortage of drugs, war conditions, etc.; 11,254 major surgical operations were performed, 6,822 maternity cases were attended including 781 for abnormal labour. The two most important hospitals are the Osmania with various special departments for both men and women, and the Victoria Zenana for women only. Both show steadily increasing work. It is proposed to construct a new mental and new Zenana hospital in the near future. A sum of 8½ lacs has been sanctioned for various works.

Ambulance classes were held and 2,037 candidates were successful in the examinations. An A.R.P. medical organization came into existence during the year, consisting of casualty and hospital services. Three hundred beds have been reserved for emergency.

#### PUBLIC HEALTH

Measures recommended for correct registration of births and deaths have not yet made satisfactory progress. The prevalence of plague, cholera and smallpox was less than in the previous quinquennium. This is particularly so in respect of plague which was responsible for 1,240 deaths against 4,498 of the previous year and the decennial average of 5,203 deaths. Of 7,530 deaths from cholera as many as 4,408 occurred in Raichur district where the infection was prevalent throughout the year. During the year 343,671 inoculations were performed. Cholera vaccine is now being manufactured in the State itself. Although deaths from smallpox were less than half the decennial average, the number of vaccinations performed, viz., 684,891, was the highest ever recorded during any one year. The Government has its own vaccine depot in Hyderabad.

**Malaria.**—Proposals have been made to expand the anti-malaria work which is at present limited to certain areas in the districts. One scheme which was sanctioned during the year brings under operation 5 towns and 120 villages with a population of 146,000, i.e. one-fifth of the total population of the district. 'This is perhaps the largest single area to be brought under malaria control in India'. Pyrocid spraying of adult mosquitoes has been introduced and a larvicidal oil prepared by mixing Diesel oil with yellow kerosene oil in the proportion of 1 : 5 is now being used in place of malariol which is unobtainable.

**Leprosy.**—Weekly clinics were held in 59 hospitals and dispensaries. The Victoria Leprosy Hospital which is meant for early cases had 830 patients at the close of the year.

**Tuberculosis.**—The construction of Ananthagiri Sanatorium continued during the year. The tuberculosis wards at two hospitals treated 760 in-patients; besides



in three clinics 66,085 out-patients attended, of whom 1,403 received artificial pneumothorax treatment. The Dabirpura Clinic, in addition to its other activities, carried intensive propaganda by home visiting, examined 1,748 contacts, x-rayed 4,035 patients and tested 2,672 sputum. All laboratory and x-ray examinations were done free of charge. The Hyderabad Tuberculosis Association was affiliated to the Central Association at Delhi during the year.

Anti-rabic treatment was given to 1,703 cases at the Chemical and Bacteriological Laboratory and at the 15 district headquarter hospitals.

Among other activities may be mentioned numerous diet surveys which showed multiple deficiencies, medical inspection of schools, maternity and child welfare work and town improvement and village development schemes. To provide adequate maternity relief four Model *Dais* Training Units have been established under the patronage of Her Highness the Princess of Berar. A scheme is now before Government for improving the sanitary conditions in villages. The City Improvement Board have spent, so far, Rs. 87,30,661 in clearing 1,000 acres of slums in Hyderabad and have several schemes in hand. The programme of constructing model houses is going on; in all 3,900 houses have been built at the cost of Rs. 47 lacs.

The report is an account of growth and progress, and shows the interest H.E.H. the Nizam's Government takes in health matters.

## Correspondence

### FLUORINE AND FLUOROSIS

SIR,—With regard to your remark 'This has led to the suggestion that non-toxic amounts of sodium fluoride may be added to drinking water for the prevention of dental decay' in the editorial of June number 1944, I wish to draw your attention to the fact that the use of fluorine in dental treatment is in vogue already. A good account was published by Prof. E. H. Lukmsky, Director, Stomatological Clinic, First Moscow State Medical Institute (fluorine cure for exposed dentine and atrophy of alveolus. *Journal of the Indian Medical Association*, Vol. X, page 483, 1941).

N. J. MOJUMDER.

29, CHAKRABERIA LANE,  
CALCUTTA.  
23rd August, 1944.

[Note.—The correspondent has missed our point. Numerous papers have appeared on the value of fluorine in dental treatment. Our reference was, as stated, to the addition of fluoride to drinking water (possibly to public water supplies) for the prevention of dental decay.—EDITOR, *I. M. G.*]

### PYROGENIC REACTIONS FOLLOWING INTRAVENOUS SALINE INFUSIONS

SIR,—I was interested in the paper entitled 'Pyrogenic reactions following intravenous saline infusions' by Drs. B. M. Paul and B. C. Chatterjee in the July issue of the *Indian Medical Gazette* (Vol. LXXIX, No. 7, p. 304). Nine years ago in the surgical wards of the Mayo Hospital, Lahore, I had occasion to give a particularly large number of intravenous saline infusions for a prolonged period. The much dreaded rigor appeared in not a few of our cases. At that time we were not aware of the results of researches carried out on a high scientific plane in later years, and referred to in the above-mentioned paper. We, therefore, like everyone else at that time incriminated successively, and later collectively, the speed with which the infusion was given (too slowly or too rapidly), the

temperature of the saline (too hot or too cold), contaminated distilled water and so on. It, therefore, became the rule for a house surgeon to prepare the infusion himself with fresh doubly-distilled water, and to give it so as to obviate all the above-mentioned factors, which were supposed to cause the rise of temperature. In spite of all that we did, and we did all that was humanly possible, cases of rigor still occurred. The routine treatment for this complication, apart from hot-water bottles, blankets, etc., was to inject subcutaneously 5 minims of 1:1,000 adrenaline hydrochloride. Later we started to add that quantity of the solution to the saline infusion prior to its injection. My impression is that we seldom, if ever, got rigor complication afterwards. Unable, in the present sphere of my work, to put this fact on a sound scientific basis, may I suggest to the writers of the above-mentioned paper to investigate the truth of this admittedly empirical remedy? In the matter of saline infusion which is unquestionably of proved efficacy, and especially when due to diverse reasons hermetically sealed pyrogen-free ampoules of saline may not always be available, it may perhaps be worthwhile to know whether the remedy suggested above has, in point of fact, any scientific basis.

M. A. SHAH, M.S.

DEPARTMENT OF  
ANATOMY, KING EDWARD  
MEDICAL COLLEGE, LAHORE,  
8th August, 1944.

### PHENAMIDINE IN THE TREATMENT OF KALA-AZAR

SIR.—During the last five months I have been testing the therapeutic efficiency of a new diamidine compound, 4 : 4'-di-( $\beta$ -hydroxy-ethane sulpho- . . . 736), in the treatment of . . . at a School of Tropical Medicine. So far 16 'ordinary' cases of kala-azar have completed the treatment with this drug, and it has been possible to obtain a clinical cure in every case. By clinical cure is meant that after specific treatment the patient became afebrile and remained so, the size of the spleen decreased markedly, the blood picture improved up to the normal level for the population, and there was a distinct gain in weight. As with other diamidines, the temperature came down to normal in most cases after the completion of a course of injections.

As in all these cases the treatment has been finished only recently, it is not possible yet to ascertain whether the cure has been permanent or not. But from the immediate results it is justifiable to conclude that the drug has a fair degree of anti-kala-azar activity.

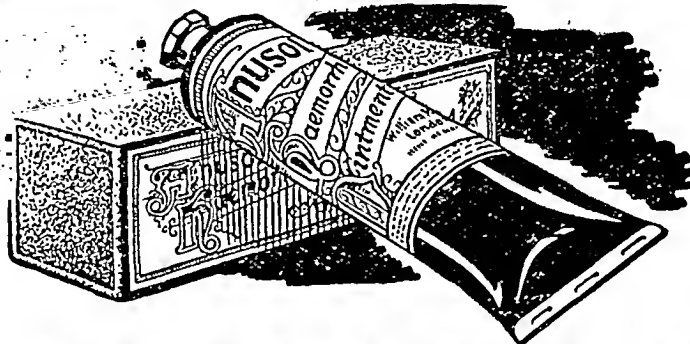
The dosage required to bring about a clinical cure was about twice the amount required with diamidino stilbene (stilbamidine, M&B 744). There has not been any very unpleasant reaction after the intravenous injections of phenamidine. The complete results of treatment of kala-azar with this drug will be published after a follow-up of the series of cases treated, six months or more after their discharge from the hospital.

P. C. SEN GUPTA, M.B. (Cal.),  
Officer-in-charge, Kala-azar Re-  
search Department, Calcutta  
School of Tropical Medicine.

CALCUTTA,  
7th September, 1944.

### PROFESSOR SIR RAM NATH CHOPRA AND THE GROWTH OF PHARMACOLOGY IN INDIA

SIR,—For the preparation of a review, I was looking through the 1942 volume of the *Indian Medical Gazette*



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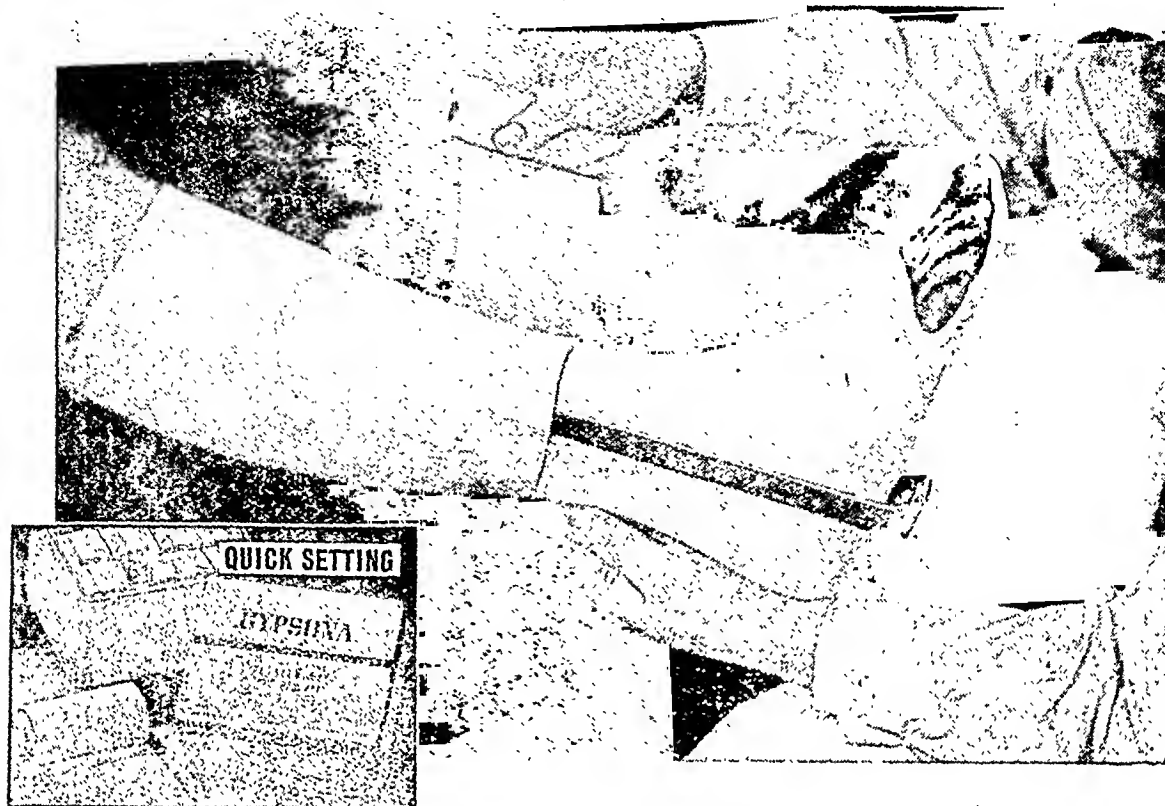
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and happened to see the article 'Professor Sir Ram Nath Chopra and the growth of pharmacology in India'. While reading this article, I noticed an inaccuracy pertaining to me. It is stated in the said article that 'Sir R. N. Chopra had . . . trained more than 45 workers in . . . pharmacology. . . . A few names would indicate the representative character of the school developed by him' (p. 369). Among the names mentioned, I was surprised to find my name, although I never had the privilege of studying under Sir R. N. Chopra. I studied pharmacology under Professor Gottlieb at the Heidelberg University where I worked on my thesis submitted for the M.D. degree of that University.

A. S. PARANJPE, M.D.,  
ch.B., D.T.M., etc.,  
Professor of Pharmacology.

SETH GOVERDHANDAS  
SUNDERDAS MEDICAL COLLEGE,  
PAREL, BOMBAY,  
1st June, 1944.

## Service Notes

### APPOINTMENTS AND TRANSFERS

MAJOR-GENERAL W. C. PATON, M.C., K.H.P., Surgeon-General with the Government of Bengal, is appointed to officiate as Director-General, Indian Medical Service, with effect from the afternoon of the 10th August, 1944, *vice* Lieutenant-General J. B. Hance, C.I.E., O.B.E., K.H.S., placed on deputation.

The services of Colonel (Local Brigadier) G. Covell, C.I.E., K.H.P., Director, Malaria Institute of India, are placed temporarily at the disposal of the War Department for employment on special military duty for a period of 5 weeks, with effect from 7th August, 1944.

Colonel G. R. Lynn, C.B.E., D.S.O., I.M.S. (retired), Additional Deputy Director-General, Indian Medical Service (Stores), whose services were temporarily placed at the disposal of Department of Supply, with effect from the 1st July, 1943, relinquished charge of his duties as Officer on Special Duty (Medical Division) in that Department on the 30th September, 1943 (afternoon), and rejoined his original post in the Office of the Director-General, Indian Medical Service, with effect from the 1st October, 1943.

The Viceroy and Governor-General has been pleased to make the following appointment on His Excellency's personal staff :—

#### To be Honorary Surgeon

Colonel J. P. Huban, O.B.E. Dated 15th April, 1944, *vice* Colonel R. Hay, C.I.E., vacated.

Lieutenant-Colonel D. Kelly, who was Medical Officer, Pachmarhi, has been re-posted as Civil Surgeon and Superintendent, Robertson Medical School, Nagpur, where he assumed charge on 6th July, 1944.

Lieutenant-Colonel D. R. Thomas, I.M.S. (retired), has been re-employed for the duration of war as Chemical Examiner to Government, Punjab, with effect from the forenoon of the 12th July, 1944.

Lieutenant-Colonel B. H. Singh, M.C., Civil Surgeon, Jalpaiguri, is appointed temporarily to act as Surgeon-General with the Government of Bengal, until further orders.

Lieutenant-Colonel J. C. Drummond, on return from leave, is appointed as Civil Surgeon, Burdwan, *vice* Dr. J. P. Datta.

Lieutenant-Colonel R. A. Wessan is appointed to be Civil Surgeon, 24-Parganas, *vice* Major J. Brebner, M.B.E.

Lieutenant-Colonel M. Das, M.C., I.M.S. (retired), is temporarily appointed as the Superintendent of the Alipore Central Jail for a period of one year, with effect from the 25th August, 1944.

Lieutenant-Colonel S. L. Patney is appointed to act as a wholetime Superintendent and Medical Officer of the Presidency Jail, with effect from the 10th September, 1944, *vice* Mr. C. A. W. Luke (retired) and Dr. Bankim Behary Roy.

Major Jaswant Singh, Assistant Director, Malaria Institute of India, is appointed to officiate as Director of the Institute, in addition to his own duties, during the absence on deputation of Colonel (Local Brigadier) G. Covell, C.I.E., K.H.P.

Major E. G. Montgomery, Civil Surgeon, Darjeeling, is appointed to be Civil Surgeon, Jalpaiguri, *vice* Lieutenant-Colonel B. H. Singh.

Major J. Brebner, M.B.E., Civil Surgeon, 24-Parganas, is appointed to be Civil Surgeon, Darjeeling, *vice* Major E. G. Montgomery.

Captain W. A. Browne, Civil Surgeon, Rajshahi, on retiring from service, is re-employed as Civil Surgeon, Rajshahi, for a period of 6 months, with effect from the 6th August, 1944, or till the termination of war whichever is earlier.

Captain A. G. T. Matthews was appointed as Medical Officer, Muscat, with effect from the forenoon of the 16th June, 1944.

The undermentioned officer retires with gratuity and is granted emergency commission from the date specified :—

#### INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Short Service Commission)

Captain K. K. Menon. Dated 22nd June, 1944.

#### INDIAN LAND FORCES

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

#### To be Captains

Sivasankaran Kumaran Menon. Dated 26th November, 1943.

Arumbalkam Visvanathier Rajagopalan. Dated 20th April, 1944.

Natampalli Anandalwar. Dated 1st May, 1944.

Brahma Prasad Sur. Dated 3rd May, 1944.

Joges Chandra Das. Dated 21st May, 1944.

Kamta Prasad Bhargava. Dated 28th May, 1944.

Dalilur-Rahman. Dated 14th June, 1944.

Mohanlal Purushottamdas Patel. Dated 8th May, 1943.

(Miss) Cochee Narayanaswamy Rukmini. Dated 8th June, 1944.

Eshai David de Kelaita. Dated 4th April, 1944.

12th May, 1944

Prabhat Kumar Haldar. Mrs. Isabel Hufiton.

15th May, 1944

Sisir Kumar Sen Gupta. Ramachandra Anant Joshi.

Birendra Narayan Ray. Usha Ranjan Ghosh.

20th May, 1944

Gummadi Seshiah. Dhroub Parkash Kapur.

#### To be Lieutenants

Dwijendra Nath Ganguly. Dated 19th March, 1944.

Bimal Kumar Roy. Dated 20th March, 1944.

Thandalam Srinivasa Bhaskaran. Dated 14th May, 1944.

15th May, 1944

Mohan Annajirao Sirur.

Ramiah Krishna Moorthy.

Bellikoth Lakshman Shenoy.

Gnanamanickan Carl Anbunathan. Dated 17th May, 1944.

20th May, 1944

Amulya Kumar Basu.

Pathiyil Raman Kutty.

Hangarkatta Shanker Nayak.

Pudukottah Subramanya Ramachandran.

Chevur Ramarao Gopinathan.

Pala Sreeramalu Babu Naidu.  
 Varaguna Pandyan Kulasekara Pandyan.  
 M. Narayanan.  
 George Paul Colaco. Dated 22nd May, 1944.  
 Varikaravadakaveetil Chathukutty Nayanar. Dated 25th May, 1944.  
 Vishwanath Brijlal Rawat. Dated 13th June, 1944.  
 Ernest Percival Eustace Denton. Dated 3rd April, 1943.

15th May, 1944

Stanley James Luxa. Ancel Percival Bedell.  
 Piers Bernard Winstanly James Edward Ferris.  
 Price.

Nahar-ud-din Ahmad. Dated 16th March, 1944.

19th March, 1944

Dakshina Ranjon Das. Chitta Ranjan De.  
 Deb Narayan Ganguly. Gobinda Chandra Bhar.  
 Tulsi Das Bhattacharya. Satchidananda Das Gupta.

20th March, 1944.

Sakti Nandan Biswas. Prabirendra Basu.  
 Rai Ranendronath Chau- Shaikh Mohamed Yousuf.  
 dhuri. Durga Das Guha Thakurta.  
 Mohammad Mamtaz-ur-Rahman. Dated 12th April, 1944.

19th April, 1944

Sunil Kumar Dhar.  
 Khagendra Narayan Brahma.  
 Tarak Chandra Sarkhel.  
 Atindra Lal Saha.  
 Anukul Chandra Roy.  
 Chittaranjan Ray. Dated 20th April, 1944.

20th May, 1944

Naranjan Dass Chhibber.

Sisir Kumar Basu.

Subodh Chandra Sarkhel.

The undermentioned I.M.S./I.A.M.C. officer has been granted emergency commission :—

#### INDIAN AIR FORCE—MEDICAL BRANCH

##### To be War Substantive Flight-Lieutenant

Captain Hassan Lakshminarayan. Dated 11th June, 1944.

The undermentioned officers have reverted to emergency cadre of I.M.S. on termination of service with the I.A.F.:—

#### INDIAN AIR FORCE—MEDICAL BRANCH

Flight-Lieutenant L. D. Kale. Dated 10th June, 1944.

Flight-Lieutenant D. P. Parakh. Dated 13th June, 1944.

Flight-Lieutenant K. B. Roy. Dated 16th June, 1944.

#### PROMOTIONS

##### Lieutenant-Colonel to be Colonel

M. L. Dhawan. Dated 18th June, 1944.

##### Majors to be Lieutenant-Colonels

G. C. Phipps. Dated 30th July, 1944.

R. A. Haythornwaite. Dated 18th August, 1944.

##### Captains to be Majors

B. S. Khurana. Dated 1st January, 1944.

N. I. McLeod. Dated 5th July, 1944.

H. J. Gibson. Dated 27th June, 1944.

#### INDIAN LAND FORCES

##### INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS

##### (Emergency Commissions)

##### Lieutenants to be Captains

M. C. J. Masters. Dated 3rd June, 1944.

V. M. Rao. Dated 5th June, 1944.

12th June, 1944

M. G. Rao. K. Dattatreya.

B. D. Kumar. Dated 15th June, 1944.

30th June, 1944

G. N. Dar.	K. N. Sharma.
M. S. Ahmed.	M. S. Malhotra.
G. Mohy-Ud-Din.	S. Z. Hasan.
D. R. Bhasin.	K. A. Sheikh.
K. L. Chopra.	M. A. A. Aziz.
S. P. Kalsy.	S. M. D. Ahmad.
M. Naqi.	M. A. Alvi.
S. M. Salim.	N. S. Brara.
M. G. Anand.	A. Singh.
S. N. Kapur.	M. Aslam.

R. A. Khan.

M. J. Van Ross. Dated 24th June, 1944.

A. W. S. Webster. Dated 27th June, 1944.

#### RETIREMENTS

Colonel C. H. N. Baker, M.C. Dated 18th June, 1944.  
 Lieutenant-Colonel Snarker Parashram Joshi. Dated 1st July, 1944.

#### RESIGNATIONS

##### INDIAN LAND FORCES

Captain Binay Bhushan Bhattacharyya. Dated 22nd May, 1944.

##### INDIAN LAND FORCES

##### INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN ARMY MEDICAL CORPS

##### (Emergency Commission)

Captain Anil Chandra Sarkar. Dated 16th May, 1944.

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## Original Articles

PSEUDO-TUBERCULOSIS OF THE LUNGS  
WITH EOSINOPHILIA, OR BENIGN  
EOSINOPHIL LEUKÆMIA

By RUDOLF TREU, M.D., L.R.C.P., etc.

Calcutta

## Introduction

SEVERAL authors have recently described the syndrome of chronic bronchitis associated with a high eosinophil blood count, symptoms of asthma, fever and loss of weight; many cases display a fairly typical x-ray appearance. Frimodt-Møller and Barton (1940), who published the first extensive description of this disease, were concerned chiefly with its x-ray appearance, but they pointed out that the condition, being essentially benign, was in no way connected with tuberculosis. However, they made no suggestions for treatment of the disease.

In February 1943, I mentioned in this journal two cases of this disease which were cured by acetylarsan. Up to 1938 only a few cases had come to my attention, none with definite radiological changes, and all were cured by 'arseno-typhoid'. None showed filaria in the blood. The curative effect of arsenicals on massive eosinophilia had actually been known to me since 1933 when the first case of this type came under my observation.

This particular patient had consulted me for fever, accompanied by a very irritant cough and swelling of the inguinal glands. His blood count showed 57 per cent eosinophil cells, and his lung skiagram was without any definite pathological change. As there was no other explanation of this high eosinophil count, I assumed it represented a rare manifestation of filariasis and treated him with 'arseno-typhoid' injections. After a few injections the symptoms disappeared, the patient became well, and his eosinophil count remained normal under my observation for years.

In January 1943, Weingarten published a detailed account of this disease, but this publication did not reach India until several months later. His study was based on eighty-one cases observed subsequent to 1934, and since 1936 he has found that the organic arsenicals were a specific. His description of the disease provided a very uniform picture: it begins with slight fever, loss of appetite and weight, and after about one week the patients develop a dry cough, especially at night; in a great number of cases asthmatic symptoms appear. Weingarten pointed out that the x-ray evidence during this early period is very distinctive, and is characterized by a mottling of the lungs, but later this x-ray appearance is not necessarily so typical. Only a small number of Weingarten's patients were females, and in no case was more than one member of a family affected. Neither he nor Frimodt-Møller and Barton noted

any example of this disease combined with tuberculosis.

In May 1943, Simeons described thirty-five cases observed in Bombay, many of which showed radiological evidence of infiltration of the lungs although others did not. Because of the absence of radiological evidence in many cases, Simeons prefers the term benign eosinophil leukæmia.

Another typical case was reported by Chaudhuri (1943) and Shah (1943), and the *Indian Medical Gazette* devoted an editorial (1943) to this syndrome.

## Recent cases

The clinical picture in the literature to date is remarkably uniform. The impression is gained that fever and cough are certainly essential symptoms of this disease. However, recent observations on nineteen new cases seen since 1943 have led me to conclude that the clinical manifestations of the syndrome are much more variable than previous records have indicated, and that the only consistent features are the high eosinophilia and the invariably dramatic results of treatment with organic arsenicals. Even fever is not an essential symptom at any stage, and the disease does not exclude active tuberculosis. Lung symptoms may be entirely absent, yet there may be gross radiological changes. The disease has now been observed in two members of the one family. The onset of the disease may be quite sudden, indicated by violent asthmatic attacks. Finally, the treatment with arsenicals may be accompanied by acute febrile reactions or symptoms of profound general malaise.

These more recent cases may be illustrated by the records of the first two patients which follow, the first displaying the typical syndrome, the second atypical in character.

*Case 1.*—European male, aged 36 years, first consultation on the 20th May, 1943. First attack of 'bronchitis' in 1939 lasting for several months. Since November 1942, had a continuous cough, very little expectoration, often with fever and breathlessness, particularly at night. Lost two stones in weight since November 1942. Clinically, the patient showed typical asthma-bronchitis; radiologically the mottling of the lungs was typical; blood eosinophilia 66 per cent; total leucocyte count 28,000.

The patient was given 2 c.c. acetylarsan on the 21st May, 1943, and 3 c.c. on the 23rd, 26th and 29th May and 1st June. Four hours after the last injection, the patient's temperature rose to 103°F. with a severe ague. Next morning the temperature was normal; no malaria parasite was found in the blood. On the 5th June another injection of acetylarsan was given, but only 1 c.c. A few hours later the temperature rose to 104°F. Again no parasite was found. Treatment was stopped after a total of only six injections. On the 3rd June the eosinophil count had come down to 13 per cent. Since his last injection the patient has had no further symptoms; his lung skiagram has become normal and has remained so. He has gained 17 pounds in weight. Eosinophil count on the 8th April, 1944, 10 per cent.

The secondary effects of arsenical treatment were much more severe in another case in which



the clinical picture failed to conform to the more or less standardized description of this syndrome.

**Case 2.**—Indian Christian male, aged 24 years, first examined on the 12th August, 1943. No history of previous severe illness. He had noticed loss of weight for some time and also an increasing feeling of weakness. Ten days previously he suddenly felt dizzy and fainted. Clinical examination: poor general state of health, thoracic organs normal, no swelling of liver or spleen; inguinal glands on the right very much enlarged but not tender—this was thought to be attributable possibly to inflammatory changes of the glands penis which was covered by hardened epithelial debris which had collected under the foreskin. The patient denied ever having had intercourse. He was advised to remove this foreign matter with some warm oil. On examination on the 14th August the glands penis looked quite normal; the inguinal glands were unchanged. His blood count showed 26,800 white cells, 80 per cent eosinophil cells. X-ray skiagram of the lungs normal.

On the 16th August treatment with acetylarsan was begun. In view of the weak general condition, only 1 c.c. was given in the first injection, but on the 18th August 2 c.c. and on the 21st August 1.5 c.c. acetylarsan were given. On the 23rd August the patient was brought to me. He was unable to walk alone and reported that since the 22nd he had had fever and very severe pain in the limbs. He had lost all appetite, was unable to raise his arms or close his fists, tendon reflexes of arms and legs were unobtainable, very slight pressure on the muscles of the extremities and particularly along the course of the extremity nerves was very painful. The condition of the patient was so alarming that he was sent to the School of Tropical Medicine, Calcutta. His eosinophil count had already fallen to 45 per cent. In hospital a tentative diagnosis of lymphogranuloma inguinale was first suggested, the diagnosis being based on the combination of fever, swelling of the inguinal glands and myositis. When the Frei test proved negative, my original diagnosis of eosinophil leukaemia with severe reaction of the type known in syphilis as Herxheimer's reaction was accepted, and the patient was dismissed after one week of symptomatic treatment. Treatment was continued with carbarsone orally. On the 8th September the eosinophil count had dropped to 13 per cent, and the swelling of the inguinal glands was much reduced. The patient has been under my continuous observation to date. He has put on 6½ pounds, feels perfectly fit for work, and his eosinophil count still fluctuates between 10 and 20 per cent.

The case described next would almost certainly have been accepted as pure eosinophil leukaemia unless an x-ray skiagram had been taken. There was no clinical indication of the necessity for this skiagram as lung symptoms were completely absent, yet the x-ray skiagram displayed the most marked changes of all the skiagrams of my series.

**Case 3.**—Anglo-Indian male, aged 17 years. First consultation on the 30th December, 1943. For a period of two weeks he had experienced irregular fever, up to 101°F. and 102°F., with a feeling of weakness and with breathlessness when running. Despite the fever the patient had not reported sick, and had continued his strenuous duties and even physical exercises, but undertook the latter with difficulty as he soon lost breath when running or jumping. There was scarcely any cough. The spleen was found to be slightly enlarged, the breath sounds over the lungs were somewhat harsh, but there was no catarrh. A diagnosis of malaria suggested by the patient and his mother appeared very likely. However, blood examination showed no malaria parasites, but 38 per cent eosinophil cells in a 21,000 total count. X-ray screening of the lungs showed very strongly diminished translucency of both lung fields, and a skiagram showed numerous and rather

large infiltration shadows spread over both lung fields (figure 1, plate XXIII). From the 2nd January to the 21st January, five injections of N.A.B. were given, 0.3 gm. each. Subsequent to the second injection the patient felt and continues to feel perfectly well. The swelling of the spleen has disappeared completely and an x-ray skiagram (figure 2, plate XXIII), taken on the 22nd February, 1944, showed the complete elimination of the pathological shadows. The eosinophil count is now 10 per cent; the total count is normal.

This baffling case, showing such extensive radiological changes of the lungs but with no clinical evidence of any lung affection, would probably not have been recognized as 'eosinophil lung' for some time. Possibly, however, some lung symptoms would have become evident after a few days, as it is not readily conceivable that such extensive changes as became evident in his skiagram could have remained latent for any length of time. Sooner or later he would presumably have experienced a sudden asthmatic attack, as in the following case.

This next case had been under my observation for some time when he suddenly developed a very severe asthmatic state, without any preliminary symptoms such as fever or cough. The x-ray skiagram showed very extensive changes which had not, of course, developed during the few days between the commencement of the attack and the date of taking the x-ray skiagram; they must have been in existence for some time before the sudden onset of asthma which led to the correct diagnosis.

**Case 4.**—Mohammedan male, aged 55 years, first consultation on the 2nd May, 1943. For a period of several years he had experienced a steady loss of weight, great thirst and increasing general weakness. Examination of the internal organs showed no pathological changes of importance; urine—specific gravity 1033, sugar 4 per cent, blood sugar 226 mg. per cent. The patient was put on diet and insulin. He gained weight fairly rapidly; blood sugar and urine sugar were well controlled. On the 13th May the patient suddenly developed a severe asthma attack, and during the following week his asthmatic fits were so continuous and troublesome that only frequent injections of adrenalin brought any relief. He was in continuous severe distress, not relieved by ephedrine. There was no fever. On the 20th May blood examination showed 47 per cent eosinophil cells, and an x-ray skiagram on the 21st May showed typical mottling of the lungs.

This case is of special interest, not only because of the sudden outbreak of severe asthma without preliminary symptoms and without fever, but more particularly because of the fact that his son, aged 5 years, was affected by the same disease. The boy had been suffering from cough with expectoration for a considerable time; an examination of the lungs indicated typical asthma-bronchitis; an x-ray skiagram showed typical mottling of the lungs, and there was blood eosinophilia of 19 per cent.

The following history is of a case in which a very sudden outbreak of a most severe type of asthma lasting for four years, again with no preliminary symptoms, and uninfluenced by the usual anti-asthmatic drugs, was dramatically cured by arsenic.

**Case 5.**—Mohammedan male, aged 43 years. This patient had been known to me for several years previous to April 1940, when he suddenly fell ill with severe asthmatic symptoms, unrelieved by the usual treatment.

He rapidly lost weight and was unable to continue his work in Calcutta. I saw him again on the 24th March, 1944. His asthmatic state had continued throughout the interval of four years, and on examination, he showed typical asthma-bronchitis, diminished breath sounds, and prolonged expiration. There was no swelling of the spleen. Blood examination—51 per cent eosinophil cells. From the 27th March to the 13th April five injections of N.A.B., 0.3 g., were given. After the third injection he suffered no further breathlessness, and examination on the 24th April gave normal breath sounds over the lungs, and there were no signs of bronchitis. The patient now feels perfectly fit, although eosinophilia of 21 per cent still persists.

Observations published to date agree that there does not appear to exist any connection between 'eosinophil lung' and tuberculosis of the lungs. Although apparently true in the vast majority of cases, this should not lead to the assumption that the one disease excludes the other, as is demonstrated by the following example.

*Case 6.*—Hindu male, aged 20 years. First consultation on the 3rd December, 1943, with a history of fever, cough, and breathlessness, particularly at night. The left tonsil showed several ulcers and typical sounds of asthma-bronchitis could be heard over the lungs. The patient was advised to rest and to take sulphanilamide tablets. When seen again on the 8th December, 1943, the tonsillitis had cleared up, but fever, cough, and breathlessness persisted. Blood examination showed 37 per cent eosinophil cells, and an x-ray skiagram of the lungs showed mottling of both lung fields, particularly below the left hilus. The broncho-vascular markings in both lung fields were strongly increased. The skiagram was not suggestive of tuberculosis, and in view of the marked eosinophilia, eosinophil infiltration of the lung was diagnosed (figure 3, plate XXIII). Under treatment with acetylsalicylic acid, breathlessness and bronchitis disappeared readily, but cough and fever persisted. On the 27th December, 1943, the eosinophilia had disappeared, and only 6 per cent eosinophil cells were found, but another x-ray skiagram (figure 4, plate XXIII) of the lungs showed diffuse loss of translucency below the left clavicle with a cavity, the mottling otherwise being less pronounced than on the previous skiagram. Sputum : T.B. positive.

The cases described above illustrate deviations from the accepted pattern of the syndrome 'eosinophil lung'. Other cases which I have observed more or less followed the typical clinical picture as described by Frimodt-Møller and Barton, Weingarten and Simeons. In a previous communication I suggested that a typical x-ray skiagram is not essential for diagnosis, just as a typical x-ray skiagram does not necessarily mean that the patient will exhibit cough and breathlessness. In several patients displaying typical clinical symptoms, I have failed to find an abnormal x-ray skiagram of the lungs. Amongst these patients was a European who had come to India in July 1942 on war service and was transferred to Calcutta in August 1943. On consulting me in November 1943, his disease had lasted for six weeks. It had obviously been recently acquired in India. All my other cases were in Indians or in Europeans who had been resident in India for many years. Assuming that the syndrome is caused by some agent peculiar to the tropics, the case of this particular European leaves a

very large margin for the incubation period. Owing to the war, a large number of Europeans have come to this country, and it is likely that some may in time develop eosinophilia and lung symptoms; it is to be hoped that observations on such cases will be made available in due course.

Weingarten concludes from his observations that the disease he describes as typical eosinophilia is found chiefly amongst people living near the sea in India. Most of my cases were residents of Calcutta, but there were several exceptions. Two patients came from Raniganj, the climate of which is not as damp as that of Calcutta, and two patients came from Bihar. One patient, a Chinese, had brought the disease from Singapore. He came to India as an evacuee, and his clinical history dated back to his Singapore days. The syndrome has apparently been observed in Australia but is very rare; under the diagnosis eosinophil leukaemia Fenner (1943) describes the case of a private, nineteen years of age, who had been treated for asthma for five years and showed a very high eosinophilia, his total blood count being about 60,000. X-ray therapy in this case remained unsuccessful, the specific effect of arsenicals apparently being unknown in Australia.

A noteworthy feature of the cases observed by me is that not one female patient occurs amongst them. Although it cannot be said that females do not suffer from this disease, it is certain that they are far less prone to attack than males.

### *Ætiology*

Until very recently no acceptable suggestions as to the ætiology of the syndrome—high eosinophil count, associated with pulmonary symptoms—have been put forward. Frimodt-Møller and Barton as well as Weingarten postulated an allergic basis, chiefly because of the common asthmatic manifestations. This theory always seemed to be open to objections. It is difficult to accept a purely allergic basis, particularly in patients who present themselves as suffering from what is obviously an infectious disease accompanied by fever, swelling of the spleen or lymph glands and eosinophilia. It is also difficult to understand why allergic manifestations so variable in nature should be consistently cured by organic arsenicals.

In a recent publication Carter, Wedd and d'Abbrera (1944) have contributed cogent evidence on the ætiology. In a large percentage of their cases which showed pulmonary symptoms they observed mites in the sputum, chiefly of the genera *Tarsonemus*, *Tyroglyphus* and *Carpoglyphus*. Some of the patients showed radiologically typical mottling of the lungs, others did not. Out of thirteen of their cases, five gave a normal blood picture, five others showed an eosinophilia from 6 to 12 per cent, and the remaining three cases showed from 38 to 66 per cent. Treatment with organic arsenicals was

erative. The authors suggest that the condition is caused, at least in part, by mite infestation of the respiratory system. This suggestion is certainly apposite in all those cases with respiratory symptoms, but in the present state of our knowledge it is not easy to see how mite infestation of the respiratory tract will cause fever, loss of weight, swelling of the spleen or lymph glands in those cases in which lung symptoms are entirely absent clinically as well as radiologically. Further, it is difficult to explain the absence of eosinophilia in such a large percentage of the above authors' cases so long as we regard high eosinophilia as essential, or even the leading feature of the syndrome. Also, it will be very difficult—apart from technical considerations—to prove mite infestation of the respiratory tract in cases showing lung symptoms but unproductive cough.

A high eosinophilia must be regarded as an essential part of the syndrome from the standpoint of therapy. High eosinophilia in combination with lung symptoms provides a definite indication for arsenical treatment. This treatment, however, failed completely to bring about any improvement in four patients who suffered from long-standing bronchitis with asthmatic symptoms and low eosinophil count, and on whom I tried this treatment as a control measure after the usual therapy directed against their asthma-bronchitis had failed previously. In every other respect these four cases might have fitted easily into the clinical picture of 'eosinophil lung'. Only observations on a very large number of cases of bronchitis with and without eosinophilia will prove how far infestation by mites is responsible for their clinical manifestation. For the present we may acknowledge that the above authors' contribution has at least thrown some light on this apparently quite common and often disabling condition.

### Summary

The syndrome of tropical eosinophilia is discussed and a number of observations described which differ from previously published records.

It is shown that lung symptoms may be entirely absent, although profound radiological changes may be present.

Clinical symptoms may be severe although unaccompanied by radiological changes of the lungs. One case is described in which there were no lung symptoms but there was swelling of lymph glands and fever.

Some reactions during the course of treatment with arsenicals are described.

Occasionally the disease may start with the sudden outbreak of violent asthmatic symptoms, unaccompanied by fever.

The occurrence of the disease in two members of the one family is noted, and an example is quoted of its association with tuberculosis.

The syndrome appears to be more widespread over India than has been assumed so far.

Its recently-suggested causation by mite infestation is discussed.

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## THE INFLUENCE OF INTRAVENOUS INJECTIONS OF QUININE ON THE MYOCARDIUM\*

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SINCE Wenkebach (1918) discovered that quinine is capable of abolishing extra systoles as well as auricular fibrillation, the attention of cardiologists has been centred mainly upon the action of this drug on disturbances of heart rhythm; this attitude was still more pronounced because of the wide use of the quinine isomer quinidine, introduced by Frey (1918) into the therapy of auricular and ventricular extra systoles, fibrillation and paroxysmal tachycardias. A large number of investigations have been devoted to the understanding of the influence of quinine and quinidine on these pathological conditions (Hecht and Zweig, 1917, Singer and Winterberg, 1921, Otto and Gold, 1926, Levine and Stevens, 1928, Schwartz and Jezer, 1934, Selherf and Siedek, 1935, Kohn and Levine, 1935, Francaviglia, 1937, Eldahl, 1940, Horine, 1940, Riseman and Linenthal, 1941); but very few facts are to be found in the literature available to us about the electrocardiographic changes which are caused by intravenous quinine administration in cases of normal heart rhythm.

In what way and to what extent does intravenously injected quinine affect the heart muscle; in what proportion of cases is myocardial damage to be expected; is an apparently normal myocardium safer against toxic quinine effects than one which shows pathological signs prior to quinine therapy? These questions have hardly been investigated with modern methods under tropical conditions. It seems to be

\* Since this article was received (August 1943), a paper bearing on the subject has appeared (*Journal of American Medical Association*, 1st January, 1944, Vol. CXXIV, p. 63) but is not available in the original.  
—EDITOR, I. M. G.

important to know to what risks a patient is subjected when the necessity arises of resorting to intravenous quinine injections.

Although it is generally recognized that this method of treatment should be reserved for the two emergencies of cerebral malaria and bilious remittent fever, in this part of the country there is a tendency to relax these limitations for the sake of a speedy effect, especially if the patients are coming from certain heavily infested areas (Mandya district) where no relative immunity exists among the population, due to the fact that this originally 'dry district' recently became a hot-bed of an extremely dangerous malaria, wiping out whole villages, as a by-effect of intensive irrigation, started about seventeen years ago.\* The educational standard of the ryots there being very low, the means of medical control up-country being insufficient, experience has proved that the patients take the quinine mixture irregularly or not at all; consequently, intravenous quinine injections, performed skilfully, became popular with practitioners and patients. Thus, it happens frequently that villagers come to the hospitals asking for anti-malarial injections, but feel disappointed and insufficiently treated if only a quinine mixture is given. This development is supported by two facts. Gross clinical observation rarely detects any untoward by-effect of slowly injected, properly diluted quinine bihydrochloride, the single doses not exceeding 10 grains (*cf.* Rao and Naidu, 1943). However, in cases treated in this way, complaints of palpitation, slight dyspnoea on exertion and lassitude during and following the series of injections are so frequent that a more detailed investigation of the cardiac condition, arising from such a therapy, seems to be justified.

#### *Method of investigation*

Twenty-four patients, five of them females, have been treated with quinine bihydrochloride by the intravenous route. The youngest was 15, the oldest 45 years of age. They all suffered from malaria only; hookworm and urinary tract infections have been excluded; this fact considerably limited the extent of this investigation series. All patients but three in whose blood falciparum crescents were found were infected with *Plasmodium vivax*. All but two had at least one typical fever attack after being admitted to the hospital, and these two afebrile cases repeatedly showed benign tertian rings in the blood. On clinical and radiological examination the heart and circulatory system was found normal or showing mild signs of a myocardial lesion, such as a muffled first sound or a slightly diminished muscle tone on fluoroscopy.

The total dosage was 40 grains, divided in 5 injections; graded doses from 5 to 10 grains

(5, 7, 8, 10, 10 grains) were administered on 5 consecutive days; each dose was injected in 10 c.c. of re-distilled water. The intravenous method of treatment was adopted for various reasons. Some of the patients stated that fever attacks recurred in spite of oral quinine administration; others complained of severe nausea, caused by the quinine mixture, or they were anxious to get rid of the fever as soon as possible and, therefore, purchased the required ampoules themselves; finally, for some time hospital stocks of quinine sulphate were exhausted, whereas some bihydrochloride was available. Cases of cerebral malaria have not been included in this series because of the impossibility of submitting them to an exertion test. Every patient was radiologically examined at the beginning and the end of the quinine course; orthodiagrams have been traced in about one half of these cases. Electrocardiograms have been taken before and immediately after exertion (climbing thrice up and down 29 steps at maximum speed) before the first and one hour after the fifth quinine injection. In one case, cardiograms have been traced before the first and after each of the following five injections. The blood pressure was estimated once before the quinine course was started and one hour after the third and fifth injection respectively.

#### *Results*

Out of 24 patients, ten had a normal electrocardiogram at the onset, fourteen showed signs of myocardial damage, having a low or iso-electric T in more than one lead. In five cases (3 men, 2 women), two of which were normal prior to quinine administration, no significant electrocardiographic changes appeared by the end of the quinine course. In five cases, all of them men, a slight improvement of the T-waves was noticed [figures 1(a) and 1(b), plate XXIV]. *Fourteen patients (11 men, 3 women), eight of whom belonged to the normal group, showed definite signs of myocardial impairment after the fifth quinine injection; in six of them, five men and one woman, the damage was considerable.* It is surprising that all these six had a normal cardiogram when treatment was started.

All the cardiographic changes were confined to the terminal deflection, causing a lowering of T which, in the seriously affected cases, became iso-electric in one or more leads. Most of these changes occurred in leads I, II and IV; if only one lead showed alterations, usually it was IV. P, P-Q and R remained unchanged. In some of these cases a depression of S-T became apparent; in others the junction became elevated or downwards convex.

Out of ten patients showing a normal electrocardiogram prior to the first quinine injection, seven responded normally to the exertion test while three gave a pathological response. Three of those who remained normal after exertion showed a considerable deterioration of the cardiogram when the quinine course was

\* Irwin Canal, built 1927 to 1931.



finished; two were not affected. The remaining two, who stood exertion well, were slightly impaired by quinine. All the three responding with a pathological exertion reaction at the onset, showed serious damage after intravenous quinine administration.

Due to the present scarcity of quinine, etc., the gradual development of the reaction from the first to the last injection could be seen only in one case. Here, the changes were most pronounced in lead IV; after two injections (12-grain of quinine bihydrochloride)  $T_1$  were very slightly lower,  $T_2$ , which originally was perfectly normal, became deeply biphasic and  $S-T_1$  elevated; after a total 20- and 40-grain respectively,  $T_1$  seemed to improve, whereas the elevation of  $S-T_1$  increased to a real 'high take off' and  $T_2$  remained biphasic. The well-known fact that quinine prolongs the electric systole, due to the increased refractory period, was noticed in almost every case.

All the alterations are certainly due to quinine and not to the malarial fever. This is clearly borne out by two cases which remained afebrile throughout the course of investigation and yet showed a considerable damage at the end of it.

In the first of them, having a perfectly normal cardiogram and a normal exertion reaction prior to quinine administration,  $T_1$  and  $T_2$  were considerably lowered,  $T_2$  became almost iso-electric and  $S-T_2$ , prior to exertion, distinctly depressed by the end of the course [figures 2(a) and 2(b), plate XXIV]. Similar manifestations of cardiac damage appeared in the other afebrile case, with the only difference that this man showed some slight pathological exertion reaction (lead II) already prior to the first injection.

No disturbance of rhythm was noticed in the course of these investigations. X-ray examination revealed some flabbiness of the heart muscle in cases in which the cardiogram showed signs of myocardial damage; slight changes in size and shape of the orthodiagram corresponded to the other findings.

A reduction of the blood pressure appeared in every case. Systolic and diastolic pressures were diminished to almost the same extent of 10 to 15 mm. Hg. after the third and not more than 15 mm. after the last injection. This reduction was noticed independently of cardiographic findings; it was present in cases in which the cardiogram improved as well as in those in which signs of a definite heart muscle lesion became manifest.

None of our patients showed serious signs of cinchonism; none manifested an idiosyncrasy towards quinine; apart from tinnitus, moderate palpitation and slight dyspnoea on exertion, no complaints were made.

### Discussion

For the proper evaluation of the results obtained by the present investigation, it is essential to summarize some of the facts concerning the fate of quinine in the organism and explaining its effect upon the circulatory system. The amount of quinine bihydrochloride excreted in the urine and the rate of elimination are about the same, whether oral, intramuscular or

intravenous administration is used. But the blood concentration, reached by intravenous injection, is by far the highest, viz 200 mg. per 1,000 c.c. blood when 0.8 gm. (about 14 grains) are intravenously injected (Clark, 1940). Though 90 per cent of the total amount leaves the blood stream in 20 minutes (Hartmann and Zila, 1918), fixation of quinine to the myocardium takes place within 30 minutes (Weisman, 1939). The depressant effect of quinine on the heart muscle was demonstrated by its action on strips of the turtle heart and the isolated frog heart; this effect is not inhibited by atropine (McGuigan, 1940). In the human heart, therapeutic doses lengthen the refractory period of auricular and ventricular muscle by 50 to 100 per cent, and considerably diminish the transmission rate. As far as the auricles are concerned, these effects are produced partly by a depression of the vagal tone, but also to some extent by a direct action upon the heart muscle, the ventricles being not under vagus influence. Finally, quinine depresses the conduction in the junctional tissue, as does quinidine as is well known. Toxic doses of both these drugs might cause auriculo-ventricular block, extra systoles, paroxysmal tachycardia and ventricular fibrillation. The last-mentioned effect is very rare; Riseman and Linenthal (*loc. cit.*) found only seven instances of it reported in literature, and all of them showed auricular fibrillation or attacks of ventricular fibrillation prior to quinine administration. Another rare, but almost always fatal, toxic effect of quinine (and quinidine) is heart standstill due to paralysis of the sino-auricular and auriculo-ventricular nodes; isolated auricular standstill was observed only during quinidine administration (Wolff and White, 1929).

Though these pharmacological actions are mainly produced by a specific action on the system and mechanism of conduction, they are partly due to a general involvement of the myocardium. Though every textbook author warns against the intravenous administration of quinine in cases of myocardial weakness, very little is known about the actual effect on the heart muscle produced by this mode of therapy, which was introduced more than fifty years ago (Bacelli, 1890). McCarrison and Cornwall (1919) and Brahmachari (1922) pointed out that a concentrated quinine solution rapidly injected by the intravenous route considerably diminishes the blood pressure. But Edmunds and Gunn (1941) state that this effect is mainly due to a depression of the vasomotor tone and to a direct action upon the muscle fibres of the peripheral blood vessels. Our observations support this explanation. We found a reduction of the blood pressure in every case of this series, whether the electrocardiogram showed improvement, deterioration or no alteration of the heart muscle. Systolic and diastolic pressures were reduced almost to the same extent, the pulse pressure remaining constant; in heart failure

due to a myocardial lesion, the diastolic pressure does not fall (Scherf and Boyd, 1939), whereas a reduction of both the pressure readings, especially of the diastolic pressure, is always found in disturbances of the tone of capillaries and small peripheral vessels (Levine, 1942). Finally, the minimum pressure in our cases was reached already when about 20 grains of quinine (one half of the total dose) had been injected, whereas the cardiographic changes, apparently, increase proportionally with the total dose administered; these facts indicate a cumulative quinine effect upon the myocardium. It seems that the mechanism which reduces the blood pressure after intravenous quinine administration is similar to that responsible for the diminished blood pressure after emetine injections (Heilig and Visveswar, 1943).

A direct proof of quinine damage done to the heart muscle in man requires electrocardiographic examination. In Anglo-American literature we have found only one reference to cardiographic changes following quinine administration. Scherf and Boyd (1940) state that quinine, like digitalis or morphine, might change the form of the terminal deflection (to which route of administration or to what dose of quinine this remark refers is not mentioned by these authors). The results reported here leave no doubt that even such doses of quinine bihydrochloride as are well within therapeutic limits have a distinctly depressant effect upon the myocardium in a high percentage of cases, a result which is rather surprising, taking into account the large doses of this drug which have been administered in cases of disturbances of the cardiac rhythm. Riseman and Linenthal (*loc. cit.*) reported two cases in which they injected up to 240 grains of quinine bihydrochloride in 48 hours, saving the life of patients suffering from ventricular fibrillation; these authors emphasize the necessity of injecting 10 to 15 grains every 2 to 2½ hours because of the rapid elimination of quinine. The significant point, apparently, is that they used the intramuscular route, while in our cases the intravenous was chosen. However, it seems important to recognize that, according to our findings, intravenously administered quinine causes more damage to a normal heart muscle than to one which already shows some lesion. Not even a normal reaction to exertion guarantees that quinine would cause no harm; though our figures are small, it seems significant that out of seven patients responding within normal limits to the exertion test, three showed a considerable and two slight quinine damage. It is in accord with these results that most of the toxic signs were found in patients 20 to 30 years old; those over 35 remained almost unaffected. Again, one is reminded of the conditions found after emetine administration; normal heart muscles showed signs of emetine toxicity in a higher percentage of cases than those with myocardial lesions (Heilig and Visveswar, *loc. cit.*). Tentatively,

one can say that less of the toxic agent is required to cause the first lesion than to increase damage already present in the heart muscle, though the reserve power and the regenerative capacity of a heart which is affected for the first time may be greater than that of the other.

The slight improvement of the electrocardiogram noticed in five cases is certainly due to the recovery of a heart muscle damaged by previous malarial attacks. Quinine contributed to this improvement only so far as it cut short the fever and thus provided a chance for spontaneous repair of the myocardium.

### Conclusion

Intravenous administration of 40 grains of quinine bihydrochloride, divided in five doses, caused myocardial damage of more or less severe degree in a high percentage of malaria cases which clinically and radiologically showed no signs of a serious pathological heart condition at the onset of the course. A normal electrocardiogram and even a physiological reaction to an exertion test are no safeguards against such toxic by-effects; therefore, this method of treatment should be used only if strictly indicated. In the ordinary case of malaria, the slightly shorter duration of the anti-malarial treatment is no compensation for the greater risk which intravenous quinine therapy involves.

### Summary

Twenty-one cases of benign tertian and three of malignant tertian malaria have been treated by intravenous administration of 40 grains of quinine bihydrochloride in five graded doses.

The electrocardiographic findings are reported and analysed.

The risks involved in this method of treatment are pointed out.

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## THE AZYGOS LOBE

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THIS short note is intended to add two more cases of 'accessory lobe of the lung (the azygos lobe)' to the total number reported so far, which does not exceed two hundred.

Wrisberg (1778) was the first to give the anatomical description of this lobe. Stibbe (1919) reviewed 23 cases from the literature including one of his own. Since 1923 radiologists have often reported this abnormality. Litten (1929) gives a frequency of 0.07 per cent, while Le Bourdelles and Jalet (1931) give 2.6 per cent for the occurrence of the azygos lobe in chest radiographs. The cases reported so far include two by Cairney (1923), fifty by Bendick and Wessler (1928), three by Emil (1929), twelve by Illig (1929), ten by Vohlmar (1930), sixteen by Jalet (1930), seventeen by Zawadowski (1930), seven by Orosz (1932), two by Cockayne (1933), one by Vita (1933), three by Bottaliga (1933) and one by Choussat (1938). Dr. P. Kesavaswamy, late radiologist, King George Hospital, Vizagapatam, showed the writer in 1939 radiographs of two cases of azygos lobe. The January issue of the *Journal of Indian Medical Association* contains reports of two more cases from the same hospital.

The two cases were discovered in an Indian general hospital during radiographic examination of patients suffering from chronic cough. The first patient, whose x-ray of the chest showed an azygos lobe (figure 1, plate XXIV), was suffering from 'eosinophil lung'. The second case (figure 2, plate XXIV) was one of chronic bronchitis. Neither of them exhibited any physical signs to suggest the presence of the accessory lobe.

## Discussion

The azygos lobe is formed by the division of the right upper lobe into two unequal portions by the azygos vein which draws a fold of the parietal pleura during the process of descent of the heart into the mediastinum in the embryo. This occurs particularly when the communicating branch to the azygos vein from the right upper limb does not disappear, as it should during that stage in the development of the embryo when the heart descends into the mediastinum. In the case of the azygos lobe, the septum is formed by both layers of the pleura, and the vena azygos lies in the groove at the base of the septum. Hjelm and Hulten (1928) call the septum 'meso'-azygos. The thin curvilinear shadow seen in the radiograph is caused by the meso-azygos in optical section. The aberrant vein may cause a dense comma-shaped shadow according to Mather and Coope (1928), or a horse-shoe shaped, pea-like, or pear-shaped shadow according to Nelson and Simon (1931). The course of the aberrant azygos vein, the shape and size of the accessory lobe will vary. Stibbe describes three types: type A in which the fissure is horizontal and cuts the lateral surface of the lung below the apex, type B, where the fissure is practically vertical and cuts the apex, and type C, in which the fissure is vertical and cuts a small tongue-shaped lobe from the medial surface of the upper lobe.

In normal circumstances, the azygos lobe is only an anatomical curiosity. It is as much liable to be diseased as any other lobe of the lung. Occasionally even when the lobe is not diseased it may give rise to altered breath sounds, impaired resonance and fine crepitations at the apex. These signs might be mistaken for signs of disease, as was seen in Mackmull's (1930) patient who on the basis of such signs was treated for tuberculosis for a period of six years and whose lung showed a normal azygos lobe *post mortem*.

The lateral wall of an apical cavity may be mistaken for the curved line of the meso-azygos. The writer has seen mediastinal hernia after left-sided pneumothorax giving rise to a similar shadow. Tomography will be useful in differential diagnosis in such circumstances.

## Summary

Available reports on the azygos lobe are reviewed. Two cases are reported. Its anatomical development is described. Its occasional importance in mistaken diagnosis is indicated.

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Fig. 1.—Anglo-Indian male, aged 17 years. Numerous and rather large infiltration shadows spread over both lung fields.



Fig. 2.—Same patient as in figure 1 after N.A.B. injections. Complete elimination of the pathological shadows.



Fig. 3.—Hindu male, aged 20 years. Not suggestive of tuberculosis; showing marked eosinophilia.

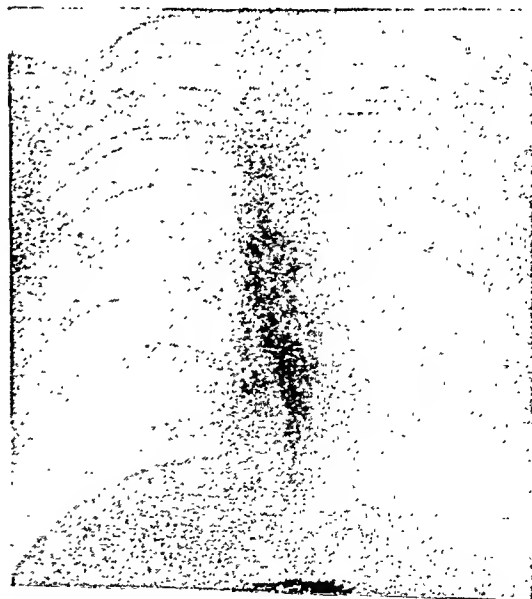


Fig. 4.—Same patient as in figure 3 after treatment with acetylarsan. Diffuse loss of translucency below the left clavicle with a cavity, the mottling otherwise being less pronounced than in figure 3.



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## ORIENTAL SORE

### ATEBRIN TREATMENT

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THE work reported here was carried out in Quetta, at the Military Hospital, and the observations, consequently, were confined to soldiers of the Indian Army.

### Incidence

Records of the number of Indian troops appearing for treatment of oriental sore at the Indian Military Hospital, Quetta, during a four-year period are shown in table I.

TABLE I

Incidence of oriental sore amongst Indian troops in Quetta

	Cases recorded at Indian Military Hospital
1936 .. .. .	458
1937 .. .. .	109
1938 .. .. .	392
1939 (first 6 months) ..	211
	1,170

Note.—The incidence increased in Quetta during the years following the earthquake of 1935.

### Prevalence

Amongst units a marked predominance seen in men of a Cavalry Unit was apparent, as is shown in table II.

TABLE II

Distribution of 500 consecutive cases of oriental sore among Military Units, 1st January, 1938 to 5th April, 1939

Cavalry Unit (mounted) ..	318 = 63.6 per cent
Three Transport Companies (with animals) ..	55 = 11.0 "
Indian Hospital Corps (located near cavalry lines) ..	49 = 9.8 "
Gunners (with few horses) ..	28 = 5.6 "
Engineers ..	14 = 2.8 "
All other units ..	36 = 7.2 "

Amongst personnel within the unit itself, infection was greatest in men whose work was most closely associated with horses, as is shown in table III.

TABLE III

Distribution of 250 consecutive Cavalry Unit cases of oriental sore among unit personnel

Syces (grooms), 'followers' ..	123 = 49.2 per cent
Sowares (riders), combatants ..	84 = 33.6 "
Other ranks, including officers ..	43 = 17.2 "

Note.—Average strength of the unit was—

Combatants ..	350
Enlisted non-combatants, 'followers' ..	200

The above tables II and III suggest the close association of those affected and the stable-fly (*Stomoxys calcitrans*), which, in addition to the sand-fly, may be an important vector of oriental sore.

### Number of sores

The number of sores on individual patients is shown in table IV.

TABLE IV

Number of sores on individual patients :  
500 cases

Single sore .. .. .	192 = 38.4 per cent
Two sores only .. .. .	120 = 24.0 "
Three to seven inclusive ..	157 = 31.4 "
More than seven sores ..	31 = 6.2 "

Note.—Single sores represent about 40 per cent of all cases. It is suggested that a single sore, naturally acquired, be allowed to run its course, if not on the face, and if protected from bites. The development of an active immunity from one infection with oriental sore is generally accepted. Inoculation with attenuated cultures of the parasite is being successfully carried out in some endemic areas.

Location of sores is shown in table V.

TABLE V

Location of sores on the body : 500 cases :  
1936 to 1938

Upper extremity (arms) ..	170 = 34.0 per cent
Lower extremities ..	69 = 13.8 "
Head (particularly face) ..	27 = 5.4 "
Trunk (alone) ..	2 = 0.4 "
'Multiple'—many types ..	179 = 35.8 "
'Multiple'—arms and legs ..	53 = 10.6 "

Note.—Exposed surfaces of the body (to which the vector has access) are the chief sites of oriental sore.

### Leishmania tropica

The presence of *Leishmania tropica* was demonstrated in approximately 40 per cent of all sores treated; e.g. 22nd February, 1939 to 29th June, 1939 of 143 cases examined at the District Laboratory, Quetta, in 57 (40 per cent) the parasite was identified. All cases here recorded were considered clinically to be of the same type.

### Bacteriology

Mention must be made of the *Neisseria micrococcus catarrhalis* as a secondary invader of an oriental sore. It has been relatively common to find this gram-negative intracellular

diplococcus in profusion being actively phagocytosed by the neutrophils of an ulcerating oriental sore. Cultures have been made in Iraq and Persia.

#### *Incubation period*

The incubation period of an oriental sore in Quetta appeared to average six months. This was computed from the mid-summer (August) preceding the appearance of a sore. The Cavalry Unit arrived in Quetta in November 1936, and the first sore was presented for treatment in December 1937, that is, after the first summer season spent in the station. The average interval between the first appearance of the sore and the time a patient reported for treatment was ten weeks.

Treatment by injection of the sore with a solution of atabrin, was being used in 1939 at a Labour Camp Hospital, by Captain I. H. B. Ghosh. The method employed was that devised by Flarer (1938). It necessitates a careful routine:

First day, hospital detention with hot potassium permanganate compresses (1/5000), four-hourly to clear secondary infection.

Second day, injection with an atabrin solution, of strength 0.05 gramme per c.c. This is done with a fine hypodermic needle inserted radially from several points on the circumference of a sore. The injection is made as superficially as possible, and as little solution is used as seems required by the size and condition of the sore. Later, injections may be

TABLE VI

*Incubation period of an oriental sore: 223 cases: the ten-weeks' development period described is subtracted*

From Aug. 1937 to Dec. 1937—One month	..	2 cases	
Jan. 1938—Two months	..	6 "	
Feb. 1938—Three "	..	21 "	= 9 per cent
Mar. 1938—Four "	..	42 "	= 18 "
Apr. 1938—Five "	..	22 "	= 9 "
May 1938—Six "	..	74 "	= 33 "
June 1938—Seven "	..	37 "	= 15 "
July 1938—Eight "	..	11 "	
2nd mid-summer to Aug. 1938—Nine "	..	8 "	

#### *Treatment*

The treatment of choice at this time in Quetta, as practised by the surgical specialist, Major D. J. P. Parker, who treated cases of oriental sore during the years under review, was 'scraping'. This consists of surface excision of a sore with a blunt spoon instrument (Volkmann's) under a short general anaesthetic. Unless deeply secondarily infected with bacteria, the wound remains superficial, and is covered with tannic acid powder and a vaseline gauze dressing weekly, which seems most satisfactory; more frequent dressings failing to speed healing. Healing time under these conditions is considered in table VII.

TABLE VII

*Healing time of a 'scraped' oriental sore: 250 cases: 1936*

One week	.. 9 cases	= 3.6 per cent
Two weeks	.. 36 "	= 14.4 "
Three "	.. 83 "	= 33.2 "
Total healed within three weeks.		51.2 per cent
Four weeks	.. 41 "	= 16.4 per cent
Five "	.. 28 "	= 11.2 "
Six "	.. 14 "	= 5.6 "
Seven "	.. 12 "	= 4.8 "
8 to 10 weeks	27 "	= 10.8 "

*Note.*—The average healing time is seen to be *four weeks*. This takes no account of the condition or type of the individual sore, and some were grossly secondarily infected.

required at three- to five-day intervals according to the response obtained. Daily dressings follow, in which the appearance of the sore determines the preparation employed, namely, a weak carbolic ointment, an ointment incorporating atabrin, or a third containing alum to stimulate healing. These are occasionally supplemented, when healing is progressing, by the application of elastoplast direct to the surface of the sore. A series of thirty-three cases, treated in this manner at the Indian Military Hospital, is considered in table VIII.

TABLE VIII

*Treatment of oriental sore by injection with atabrin: thirty-three consecutive cases with eighty-seven sores: 1939*

Cases with single sore	..	18 cases
Cases with multiple sores	..	15 "
Average interval between first appearance of sore and time of presentation for treatment was <i>ten weeks</i> . The parasite was identified in 18 cases (54 per cent of this series).		
Upper extremities alone affected	..	15 cases
Lower extremities alone affected	..	6 "
Multiple sores on the individual	..	12 "
Head involved (face ideal for this treatment)	..	8 "
Of 87 sores, 62 (71 per cent) were unbroken, non-ulcerating: suitable.		
Number of cases requiring—		
One injection only	..	10
Two injections	..	11
Three injections	..	9
Four injections	..	3

Healing time is shown in table IX.

TABLE IX

Healing time of an oriental sore injected with atebtrin

One week ..	.. No cases	= 12 per cent
Two weeks ..	.. 4 "	= 24 "
Three " ..	.. 8 "	= 24 "
Total healed within three weeks.		36 per cent
Four weeks ..	.. 10 "	= 31 per cent
Five " ..	.. 7 "	= 21 "
6 to 9 weeks ..	.. 4 "	= 12 "

Note.—The average healing time for all types was four weeks.

Comparison of the two methods of treatment of an oriental sore considered here is shown in table X.

TABLE X

Comparison of two methods of treatment considered

	Injection	'Scraping'
General anæsthetic ..	.. None	Required
Hospital detention ..	.. Desirable	No
Subsequent care ..	.. Daily	Weekly
Suitable sore ..	.. Best non-ulcerating.	Any stage
Average healing time ..	.. Four weeks	Four weeks
Resultant scar ..	.. Minimal	Good

#### Discussion

'Scraping' requires a short general anæsthetic. Local injection with an atebtrin solution produces some anæsthesia itself. 'Scraped' cases are given little preliminary antiseptic care. Injected cases require hospital detention, at least desirably, for initial antiseptic treatment. Both cases may, however, demand hospitalization if grossly secondarily infected at any stage of treatment. 'Scraping' can be applied to any oriental sore. Injection is most suitable for sores with as yet unbroken skin. In the reported series of eighty-seven injected sores, sixty-two (71 per cent) were in the non-ulcerating, relatively early papular stage.

The healing time of the two treatments appears to be about equal, each averaging four weeks. Of 'scraped' cases, 50 per cent healed within three weeks, and the remainder took longer periods. Of the small series of injected cases considered, only 36 per cent healed within three weeks, but the general average was as good. The resultant scar following 'scraping' becomes eventually almost unnoticeable, but its hyperæmia may persist for a protracted period. The scar of an injected sore is minimal.

Summary, from observations in Quetta, 1939.

1. Exposed surfaces of the body, particularly the arms, are the commonest sites of oriental sore.

2. Single sores represent about 40 per cent of cases, multiple sores 60 per cent.

3. *Leishmania tropica* are demonstrable in at least 40 per cent of all typical oriental sores.

4. The prevalence of infection amongst military personnel is greatest in those in close contact with animals, suggesting the stable-fly (*Stomoxys calcitrans*) as a vector, as well as the sand-fly.

5. The incubation period appears to average six months.

6. Two methods of treatment are compared, whose healing time appears to be about equal, within four weeks. Injection with an atebtrin solution is an ideal treatment for early, non-ulcerating oriental sores, particularly on the face. 'Scraping' is a method of choice applicable to all stages.

#### Acknowledgments

I wish to acknowledge the previous work of Major D. J. P. Parker, and Captain I. H. B. Ghosh, and to thank Major-General Cursetjee, D.S.O., who detailed me to compile this review, and Colonel J. R. Dogra, M.D., A.D.M.S., who has helped to arrange and encourage me to submit it for publication now.

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## TROPICAL ULCER IN ANGUL, ORISSA

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#### Introduction

BESIDES the Naga regions of Assam, tropical ulcer was not generally known to occur elsewhere in India.\* Recently its occurrence in several places in Orissa has been seen, particularly at Angul, where the disease has been studied in some detail. Since the disease has been recently introduced into Angul, it may be interesting to report on its introduction, its spread, its subsidence and recrudescence, its predilection to particular groups of people, and its response to various lines of treatment.

#### Topography and climatology of Angul

Angul is the headquarter station of the small backward and sparsely populated sub-division of the Cuttack district. It is situated on an undulating plain surrounded by hills and jungles. Other details are given below :—

Area of the town ..	2.92 square miles.
Population ..	2,766 (with an extra fluctuating population of 2,000).
Density ..	947.3 per square mile.
Latitude ..	20° 45' N.
Longitude ..	85° 3' E.
Altitude ..	455 feet above sea level.
Distance from the sea ..	About 200 miles.
Monsoon ..	June to October.
Rainfall ..	50 to 60 inches.
Temperature ..	Highest mean maximum 108°F. (June 1942). Lowest mean maximum 80°F. (December 1942).

\* Reports on tropical ulcer in many different parts of India have recently been seen by me; several have been submitted for publication in this journal. It has been possible to publish only a few.—EDITOR, I.M.G.



The following disease-carrying insects are found: the house-fly, mosquitoes, culex and anopheles, and ticks in neighbouring jungles.

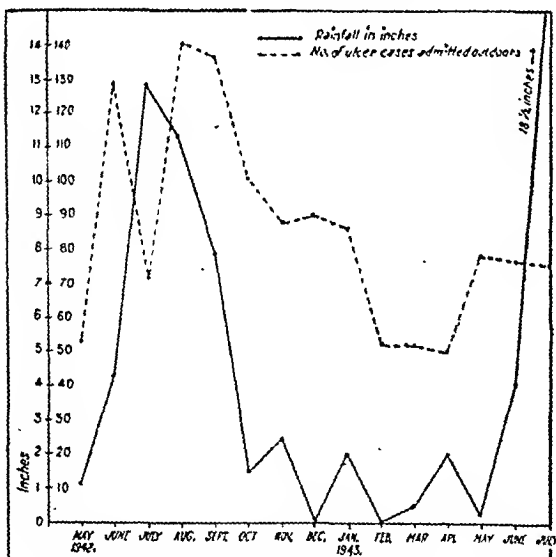
The common diseases are malaria, leprosy, malnutrition, filariasis, yaws (a few cases from the neighbouring hilly area). A few cases of endemic typhus are reported.

#### *History of introduction of the disease into Angul*

No case of tropical ulcer is known to have occurred in Angul prior to May 1942, when the first authenticated case came under notice in a fairly healthy and robust labourer who got the disease while working as a coolie in Assam. He was admitted into the Angul Sub-Divisional Hospital for treatment on the 29th May, 1942. Since then, there has been a steady stream of cases with no history of having ever been to the known endemic areas. Of them, 90 in-patients were selected for special duty. A short description of the ætiological factors, symptomatology and lines of treatment is given below. Tables and graphs are also appended. These relate mostly to the indoor cases.

#### *Seasonal prevalence*

The disease showed a seasonal prevalence. Beginning from mid-summer (May 1942), the number of indoor and outdoor admissions went on increasing, reaching the peak in August-September 1942. There was then a progressive decline, with a smaller rise in April-May 1943. The rise and fall in the incidence of the disease



generally follow the monthly rainfall. This has been shown in the graph.

#### *Incidence in relation to age and sex*

The most active period of adult life appeared to be very favourable for the occurrence of the disease. The age distribution of the cases of the disease is given below:—

TABLE I

					Total
Age	15-24	25-34	35-44	45-54	
Males	63	16	5	4	88
Females	..	..	..	2	2
	63	16	5	6	90

Males greatly preponderate over the females. There were only two females as against 88 males in this series of 90 cases.

#### *Incidence in relation to occupation*

Most of the patients in this series followed occupations which exacted very hard strenuous physical labour as shown below:—

TABLE II

UNDER TRAINING				Day labourers	Others	Total
Constables	Havildars	Police officers	Civil pioneers			
46	2	4	24	8	6	90

#### *Incidence in relation to economic status and housing conditions*

The general economic condition, social status and mode of housing appeared to play an important part in the ætiology of the disease. Comparatively poorer classes and lower social groups were mostly affected. Persons of the officers rank, although living intimately associated in the same surroundings, usually escaped from the disease. The disease has been found more or less local. Closely crowded and insanitary housing and unclean habits tended to increase the incidence. In the suburbs of Angul with sparsely populated localities, the disease incidence is very low even among the poor day-labourers, both agricultural and non-agricultural.

#### *Predisposing causes*

*General health and nutrition.*—The general health and the state of nutrition appeared to play some part. Lowered vitality, malnutrition, chronic malaria, hookworm disease was often associated with the disease; nevertheless, a number of healthy or robust persons developed such ulcers. Persistence of the disease was more pronounced among the unhealthy than among the healthy people.

#### *Exciting causes*

In the immediate ætiology of the ulcers, trauma formed a very important factor.

Traumatic or otherwise, any breach of continuity of skin surface appeared to be one of the exciting causes of the tropical ulcer. Ordinary ulcers, scabies, eczema, and furunculosis appear to have provided a suitable portal of entry of the causative organism. The poorer class of people subjected to hard outdoor physical work are more liable to trauma. Moreover, dirty and unhygienic living plus the usual neglect in the initial stage of the ulcer are the contributory factors in the occurrence of these tropical ulcers. The possible presence of the infection in the soil, water and fomites, as also close contact with infected people, may contribute to aetiology.

#### *Regions of the body affected*

The lower limbs invariably below the knee were found to be the commonest site for the tropical ulcer. Only a few cases had, in addition, an ulcer on the upper limb. This was probably due to auto-infection by inoculation. These ulcers in the upper limbs occurred after the lower limbs were affected. The dorsum of the foot was found most frequently affected. The ulcers were sometimes single, sometimes multiple.

#### *Bacteriological findings*

Bacteriological examination of the ulcers was made only by microscopic examination of smears made from pus, slough, scrapings from the base of the ulcer and from punctures at the margin. The smears were usually stained by Boye's technique as developed by Sineons (1942) at Satara. Some smears were stained by Gram's method, or Ziehl-Neelsen's method. In the limited scope of the bacteriological examination, fusiform bacilli, Vincent's spirochaetes, diplococci, streptococci and staphylococci were found in the ulcers. To none of these could definitely be assigned the definite rôle of being the causative organism. Their incidence in the ulcers is given below in a tabulated form (table III); diphtheroids were also recognized in later cases not included in this series.

These include diphtheroids, *Micrococcus catarrhalis*, *Bacillus subtilis* and some fungal organisms. The incidence of these organisms has been investigated later by my colleague Dr. J. K. Mahanty.

#### *Symptomatology and progress*

Like the ordinary ulcers, four fairly well-marked stages, namely, early, sloughing or spreading, indolent, and healing stages, were discerned, although the exact transition between the stages was indefinite. The appearance and behaviour of the disease in various stages were not on the whole very different from those described in the textbooks or by other workers. The prominent points as seen here in the different stages are briefly referred to below:—

*Early stage.*—Indistinguishable from ordinary ulcers except on bacteriological examination; a small amount of sloughy pus seen sometimes in the undermined edges.

*Sloughing stage.*—Unhealthy-looking ulcers covered over with foul smelling sloughy pus not adherent to the base of the ulcer; margins clean-cut or punched-out or sometimes overhanging like a gummatous ulcer; bacteriologically positive; the sloughing process goes on extending laterally and deep, day by day.

*Indolent stage.*—Exudation continues with no more sloughing and spreading; ulcer-margin distinct but not steep cut; base slowly merging on the surrounding skin surface; unhealthy granulation; bacteriologically positive; long duration.

*Healing stage.*—Indistinguishable from ordinary healing ulcer; no sloughy exudation; ulcer flush with skin surface; slow progress with epithelization, tendency to scar formation; bacteriologically negative except a few diplococci now and then.

In favourable cases, the indolent stage was avoided, the ulcer passed from the sloughing stage to the healing stage. Healing was rapid in these cases. In some cases, fresh trauma-

TABLE III

	Total number	Fusiform bacillus	Fusiform bacillus, Vincent's spirochaete	Fusiform bacillus, Vincent's spirochaete, diplococcus	Fusiform bacillus, diplococcus	Diplococcus	Negative
Number of cases examined ..	72	16	4	4	23	12	13
Number of examinations made	144	52	8	2	28	20	34

Streptococci in short chains and staphylococci were met with in many cases, associated with one or the other of the above groups. Their incidence has not been separately assessed. Lately, organisms other than those already referred to have been found in some ulcers.

tization led to flaring up of the ulcer and the whole process was repeated over again.

In the great majority of cases, there was little or no fever, no marked leucocytosis. The neighbouring glands were not affected in most cases. The ulcers were seldom muscle-deep.

TABLE IV

*Different lines of treatment and their effect on the duration of the disease*

Line of treatment	Number of cases	Procedure	General response	Average duration of treatment, days	Average duration of disease, days	REMARKS
1	2	3	4	5	6	7
(1) Sulphapyridine	12	Crushed M&B 693 tablets rubbed into the ulcer after the preliminary preparation. Two per cent sulphapyridine ointment applied in later stages. Oral sulphapyridine in few cases only which were of serious nature. With commencement of healing, sterilized vaseline dressing.	Usually the initial response good : sloughing process stopped. Response in indolent stage less satisfactory. Retarded healing process in the healing stage particularly with prolonged local use with bigger doses : seems to be not only bacteriostatic but tissue-static also.	21.6	31.3	Did not appear specific but definitely reduced the duration of the stages.  Local application in small dosage for a few days seems to be the ideal method.
(2) Sulphanilamide	8	Bisulphanilamide tablet crushed applied as above.	Definitely better and quicker response : quicker disappearance of organisms in smears.	11.6	22.2	
(3) Hydrarg. perchlor.	11	Ulcers cleaned with 1 in 1,000 lotion and dressed with gauze soaked in the same : or ulcer was dressed 1 to 2 per cent ointment alone. Subsequent sterilized vaseline dressing.	Response quick and satisfactory. Early disappearance of organisms. No indolence seen.	14.8	23.9	No other mercurial preparation tried.
(4) Permanganate of potash and acriflavin.	8	After cleaning, the ulcers were painted with 2 per cent potass. permanganate lotion and dressed with gauze soaked in 1 in 1,000 acriflavin.	Response very unsatisfactory in all stages.	18.8	28.8	
(5) Copper sulphate.	6	After the usual initial cleaning the ulcers were rubbed with copper sulphate crystals or dressed with 5 per cent ointment followed by vaseline dressing later.	Response very satisfactory in indolent stage : applied early, indolence prevented.	27.6	68.3	This refers to cases treated with copper sulphate solely. In other cases, it was used whenever exuberant granulation was found.
(6) Turmeric	6	Applied as a powder, paste or poultice on ulcer previously cleaned.	Initial cleaning with no satisfactory subsequent response.	25.6	35.6	Served as a good deodorant. Warm poultice encourages tissue growth.
(7) Mag. sulph.	7	Exsiccated mag. sulph. crystals applied directly over the ulcer day by day till sloughs cleared up.	Very unsatisfactory : seemed to retard healing.	31.0	49.0	

TABLE IV—concl'd.

Line of treatment	Number of cases	Procedure	General response	Average duration of treatment, days	Average duration of disease, days	REMARKS
1	2	3	4	5	6	7
(8) Pyrogenesis	13	Artificial fever was caused by intramuscular injection of sulphosin or of milk.	No particular advantage was seen with very high fevers repeated at intervals.	27.0	42.0	Sulphur 10 grains. Arachis oil—1 oz. 1 c.c. injected intramuscularly.
(9) Unclassified mixed treatment.	17	As the exigencies of the situation required the line of treatment was changed. In some cases, ulcers were excised; sulphapyridine applied and copper sulphate was applied late.	There was no particular advantage seen.	43.8	62.6	Here the different lines of treatment got mixed up. Response could not be assessed.
(10) No treatment	2	Definite cases of tropical ulcer with fusiform bacilli, Vincent's spirochaetes and diplococci left hospital after diagnosis and seen again on recovery.		75.5	75.5	Accidental controls.
	90					

In the one fatal case, there was progressive gangrene of the foot and leg; amputation was refused.

Pain was not at all an important symptom, but tenderness of the ulcer was extreme, and dressing of such ulcers was a trying job.

The ulcers usually healed by light scab formation or complete epithelization. The resulting scar was healthy, supple, not adherent to the subcutaneous tissues. In long-standing and neglected cases, a hard raised scar or keloid resulted, adherent to the deeper tissues. Very rarely there were contractures. Relapses have been seen to occur; but recurrence of the ulcer on the healed scar has not yet been seen.

Of the 90 cases admitted from May 1942 to July 1943 and studied, 8 cases were admitted in the early stage, 70 cases in the sloughing stage, 12 cases in the indolent stage, no cases were admitted in the healing stage.

The average duration of the disease from onset to recovery was long and variable, and so also the duration of the stage. No useful average could be calculated. However, the average duration of the two untreated cases has been 75.5 days.

#### Treatment

*General.*—The cases on admission were put on general hospital diet supplemented by milk and eggs when the patient could afford them. In addition, the patients were given sprouting

green gram (moong), amla powder, rice polishings, shark liver oil and calcium lactate in the form of an emulsion. Anæmic patients were given iron. Associated diseases such as chronic malaria, hookworm disease were treated in the usual way.

*Local and special treatment.*—The ulcers were cleaned thoroughly usually with weak Condy's lotion or saline. Overhanging margins were excised, or the ulcer lightly scraped if necessary. The case was put on any one of the lines of local and special treatment shown in a tabulated form (table IV). Several days' interval between dressings was usually given unless the sloughy discharge was copious. This did not produce any deleterious effect on the healing of the ulcer; in fact, the effect was favourable. When the indolent stage was reached and unhealthy and exuberant granulation was seen, copper sulphate cauterization or copper sulphate (5 per cent) ointment was applied. The response to the different lines of treatment has been tabulated in table IV.

#### Discussion

In the wider ætiology of the ulcers, the observations in this series of cases generally agree with those of other workers in so far as their prevalence, in the monsoon and the influence of poverty, hard trying outdoor physical occupations, exposure to injury of the lower limbs are concerned. Malnutrition and

deficient diet, particularly calcium deficiency, do not seem to be very important ætiological factors. A large number of cases of this series were in well-nourished robust young men with no well-marked ill-balanced diet. Trauma, breach of continuity of skin surface, infection and neglect seem to be the predominant causative factors of tropical ulcer. Clements (1934, 1936) working in Papua, Manus and New Guinea suggests that deficient diet predisposes to the easy establishment of the invading organisms. But malnutrition, like any other condition causing impaired vitality, must be regarded as a predisposing factor not only to the tropical ulcer but all diseases zymotic or otherwise.

Organisms such as fusiform bacilli, Vincent's spirochaetes, diphtheria and diphtheroids and diplococci have been incriminated from time to time as causal organisms. No definite conclusion has yet been reached.

In the present Angul series of cases, fusiform bacilli alone or associated with Vincent's spirochaetes, diplococci, streptococci, and staphylococci, were found in a large number of cases in the smears made from pus and scrapings from the base of the ulcer. In a fairly large number of cases, gram-positive diplococci (both intracellular and extracellular) were found alone or associated with other organisms. In some cases, the diplococcus was found persisting for a long time even in the healing stage when other organisms had disappeared. The presence of diphtheroids has been recognized in some cases, but no case of diphtheritic palsy or neuritis has been encountered in the present series of cases. (A greater incidence of diphtheroids has been shown in a subsequent investigation at Angul by my colleague Dr. J. K. Mahanty.)

No specific treatment has yet been discovered or evolved for these ulcers. Heroic procedures such as quick liquefaction of the slough by pure carbolic acid and the complete excision of the ulcer have been suggested in the past. In the present series of cases, complete excision under local anaesthesia was tried, but in spite of it the sloughing process continued unless sulphapyridine or sulphanilamide was used after the excision. Even then, results were not satisfactory.

Medical workers of the Assam tea gardens favourably report on sulphapyridine. In the present series, cocci, fusiform bacilli, spirochaetes and other organisms quickly disappeared with local sulphapyridine treatment, but healing appeared to be delayed. Costly sulphapyridine has no particular advantages over the cheaper sulphanilamide.

On the supposed relationship with syphilis, intravenous N.A.B. has been used. It produced no specific effect; local N.A.B. suggested itself but it could not be tried for want of supplies.

As suggested by Rogers and McGaw (1935) perchloride of mercury either in the form of 1

in 1,000 lotion or 2 per cent ointment yielded very encouraging results.

### Conclusions

The study of this series of 90 indoor cases and general observations on about 1,278 outdoor cases lead to following tentative conclusions:—

1. Tropical ulcer was introduced into the non-endemic area of Angul from the endemic area of Assam. All the prerequisites of the disease being present in the new place, it spread here widely, and it appears to have established itself in its new home. It has been spreading in other parts of Orissa also.

2. Though the actual causal organism has not been identified, it appears to be definitely infective. Trauma, breach of continuity of skin surface, infection and neglect plus unhygienic living are the causative factors of the disease.

3. Untreated and neglected, the ulcer takes a very long period to heal. Under treatment, the duration is definitely cut short. Neglect and fresh traumatization flare up the healing ulcer and favour relapse.

4. Sulphanilamide and sulphapyridine are very effective in the early stage. They are quite satisfactory in the sloughing stage. In the indolent stage, they fail to influence the course of the ulcers. In the healing stage, they tend to retard healing. Sulphapyridine has no particular advantage over sulphanilamide. Oral administration has no particular advantage. Local application is not only more economical but more effective. Application in the form of an ointment seems to be useful.

5. Copper sulphate is very effective in the indolent stage. Perchloride of mercury as a 2 per cent ointment seems to be quite satisfactory in all stages except in the healing stage.

6. Applications of magnesium sulphate, excision and pyrogenesis are by themselves alone useless unless accompanied by other methods of treatment.

### Acknowledgment

I am grateful to Lieut.-Colonel A. N. Chopra, Director of Health and Inspector-General of Prisons, Orissa, for his encouragement and for the departmental permission to publish this report. My special thanks are due to Dr. G. Panja, Professor of Pathology and Bacteriology, Calcutta School of Tropical Medicine, for his invaluable help and encouragement and for confirming our diagnosis and for his comments and suggestions. I am also grateful to Dr. B. Patnaik, Bacteriologist and Pathologist to the Government of Orissa, for investigation of certain of our cases. Finally, my thanks are due to my colleagues Dr. J. K. Mahanty and Dr. (Miss) A. P. Puri, for their help and collaboration, and to the latter for her help in the laboratory work.

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# TREATMENT OF SIMIAN MALARIA (*P. KNOWLESI*) WITH STILBAMIDINE —M&B 744

By B. M. DAS GUPTA

and

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STILBAMIDINE (4:4'diamidino-stilbene) does not appear to have been tried in malaria of man or animals. The present trials were prompted by the finding that malaria seldom occurs in kala-azar cases during treatment with this drug, whereas it does in cases treated with antimony compounds (personal communication from Dr. P. C. Sen Gupta, kala-azar research worker in this institution).

## Methods

Our general methods in testing antimalarials against *P. knowlesi* in rhesus monkeys have been described elsewhere (Das Gupta and Siddons, 1943). In the present trials, monkeys weighing 1½ to 6 kilos were treated during the patent period of the primary infection with dosages of stilbamidine varying from 0.001 to 0.005 gm. per kilo of body-weight. The drug was administered once daily by the intravenous injection of 1 to 4 c.cm. of solutions in distilled water. In the interests of economy, strict control animals were not used, but during the period of these experiments ample evidence was obtained that the strain of *P. knowlesi* had lost none of its virulence.

TABLE  
*Action of 'stilbamidine' in simian malaria (P. knowlesi)*

Monkey number	Dosage : gm. per kilo of body-weight	Number of daily doses by amt. per dose, gm.	PERCENTAGE INFECTION OF R.B.C.		REMARKS
			Before treatment	After treatment	
1	0.001	5 × 0.003	14.0	0.1	Blood negative 3 days after treatment. No relapse up to 7 months later.
2	0.001	2 × 0.004	15.6	42.0	Died.
3	0.001	7 × 0.004	3.8	0.0	Relapsed after 8 days. Retreated, relapsed again; chronic infection established.
4	0.001	6 × 0.004	0.8	0.0	During treatment count reached 12.8 per cent. Relapsed after 13 days; chronic infection established.
5	0.001	5 × 0.004	1.4	0.0	During treatment count reached 9 per cent. Relapsed after 9 days; chronic infection after treatment.
6	0.001	5 × 0.003	1.0	0.1	During treatment count reached 5 per cent. Blood negative 2 days after treatment. Relapsed after 16 days with a chronic infection.
7	0.001	5 × 0.002	2.0	0.1	Count reached 6 per cent. Blood negative 2 days after treatment. Relapsed 7 days later. Retreated; chronic infection.
8	0.001	8 × 0.001 3 × 0.003	0.4	1.0	Count reached 11 per cent after 3rd dose before a persistent, low-grade infection was established. Monkey weighed 2½ kilos.
9	0.002	5 × 0.007	2.0	0.0	No relapse up to 117 days after treatment.
10	0.002	6 × 0.01	4.0	0.0	Count reached 21.8 per cent infection during treatment. During 63 days after treatment, parasites seen once only.
11	0.002	1 × 0.008	14.6	?	Animal found dead next morning after treatment. Parasites appeared to have increased.
12	0.002	6 × 0.01	7.4	0.0	During 62 days after treatment parasites seen once only after 51 days.
13	0.002	1 × 0.012	11.2	?	Found dead morning after treatment.
14	0.0025	6 × 0.01	12.0	2.0	Count reached 52 per cent before infection was controlled. Animal died on last day of treatment.
15	0.0025	7 × 0.04	5.0	0.0	Relapsed with low-grade infection 7 days later. Intravenous treatment not entirely successful owing to collapsed, flabby condition of blood vessels; treatment partly intramuscular.
16	0.0025	6 × 0.005	1.0	0.0	Relapsed with low-grade infection 16 days later.
17	0.003	6 × 0.005	3.2	0.0	Count reached 9.4 per cent infection. No relapse up to 47 days after treatment.
18	0.003	6 × 0.006	24.8	0.0	No relapse up to 40 days after treatment.
19	0.005	5 × 0.0175	3.6	0.0	Blood negative after 4 doses. No relapse up to 31 days after treatment.
20	0.005	4 × 0.01	30.2	0.1	Blood negative 2 days after treatment. No relapse up to 31 days after treatment.



### Observations

The essential experimental data are given in the table. They show that 16 out of 20 monkeys survived the primary infection of *P. knowlesi* after treatment with stilbamidine. The failures occurred with a comparatively small dosage when the infection rate of the red cells exceeded 10 per cent. The results with monkey no. 1 appear exceptional and could not be confirmed, for, with dosages up to 0.0025 gm. per kilo of body-weight, the parasites usually increased during the first three days of treatment. The higher dosages controlled the infections with over 20 per cent of the red cells parasitized. The parasites showed degenerative changes, though a rapid action was apparent only with the higher dosages.

An interesting feature is the low relapse rate with dosages of 0.002 gm. per kilo and over (monkeys nos. 9 to 19). If the transient reappearance of parasites on a single occasion in monkeys no. 10 and no. 12 is not regarded as indicating relapse, and if monkey no. 15, which was not satisfactorily treated, is excluded for the present purpose, the relapse rate is 1 in 8 or 12.5 per cent. None of the 4 animals treated with 0.003 to 0.005 gm. per kilo have shown relapse. Whether the drug effects a radical cure has not yet been determined. Parasites have not been observed in smears of bone marrow of monkeys showing no relapse.

### Conclusions and comments

These trials show that stilbamidine possesses potent antimalarial properties. The low relapse rate is noteworthy. After atebirin, the relapse rate of *P. knowlesi* infection is practically 100 per cent, and even after 5 days' intensive treatment, the relapse may be as severe as the primary infection (Chopra and Das Gupta, 1933); treatment with small doses (using atebirin or mepacrine) over a longer period does not appear to affect the relapse rate (Das Gupta and Siddons, 1943). After quinine treatment, *P. knowlesi* infections relapsed at the rate of 2 in 12, or 16.7 per cent, and such relapses can be of fatal intensity as late as four months after the control of the primary infection (Chopra and Das Gupta, 1934). Unfortunately, stilbamidine in human beings has been found to produce some untoward neurological effects (Napier and Sen Gupta, 1942) so that trial in human malaria is not recommended.\*

### Summary

Trials with stilbamidine—M&B 744 against *P. knowlesi* in rhesus monkeys are reported. Sixteen out of twenty monkeys survived the primary infection of a virulent strain of that parasite when treated with dosages varying

from 0.001 to 0.005 gm. per kilo of body-weight. A parasitocidal action was evident, and the relapse rate was 12.5 per cent in 8 animals treated with dosages of 0.002 gm., or more, per kilo of body-weight.

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## OBSERVATIONS ON MALARIA COMPLICATING KALA-AZAR

By P. C. SEN GUPTA, M.B. (Cal.)

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ENQUIRIES have recently been addressed to the writer as to whether malaria and kala-azar can co-exist, and whether it is possible for a patient to suffer from malaria during the course of treatment for kala-azar. The question has also been raised whether the antimonials used in the treatment of kala-azar have any therapeutic action on malaria. In this communication it is intended to discuss these questions in the light of recent clinical experience in hospital practice.

### Malaria complicating kala-azar

That malaria may complicate kala-azar was recognized by the early workers on kala-azar in this country. Napier (1927) remarked that plasmodial and leishmanial infection must co-exist in the same patient very frequently, but the occasions on which both parasites would be found in the same film of either peripheral blood or spleen puncture material were few. Malarial attacks were uncommon when a patient was suffering from kala-azar, but once the disease was under control, a typical attack of malaria was not uncommon. On the other hand, Brahmachari (1928) was of the opinion that malaria complicating kala-azar did not occur so often as one would expect from the common endemicity of the two diseases. He attributed this to the intake of quinine by the patients prior to coming under observation for kala-azar. He found that in hospital practice malaria was rarely found as a complication of kala-azar.

Brief notes of a few recent hospital cases of kala-azar complicated with malaria are presented to show the clinical features of this complication.

### I. Cases showing malarial infection prior to specific treatment for leishmaniasis

Case 1.—B. K. M., an Indian male, aged 22 years, was admitted on 20th August, 1943, for recurring attacks of fever for two years. He had been diagnosed as kala-azar and was treated with several courses of different antimonials and one course of M&B 800, but he relapsed within a short time of completion of each

\*This objection to trials in human malaria does not appear valid. These neurological complications have been reported after prolonged administration, and in any case are not dangerous. Trials of the drug in human malaria are now being carried out.—EDDON,

course of treatment. On admission, the patient was found to be weak and anæmic; the spleen was hard and enlarged up to 8½ inches below the tip of the 9th left costal cartilage, and the liver was just palpable. The heart was pushed up, the apex beat being in the 3rd left intercostal space on the nipple line. There was slight bronchitis. No other abnormality noted. The aldehyde, antimony, and complement-fixation (for kala-azar) tests were positive. Malarial parasites (scanty rings) were found in the thick film. The patient was put on a course of quinine—but this did not have any effect on the fever (see figure 1). The malarial parasites disappeared with the commencement

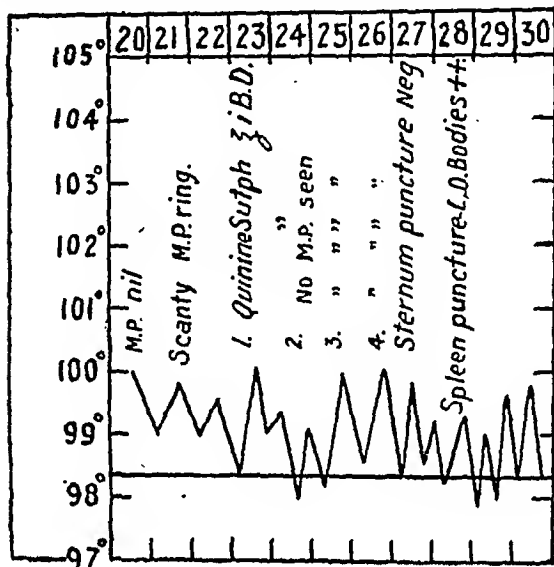


Fig. 1.—Case 1.

of quinine therapy. A spleen puncture subsequently showed numerous leishmania, and the patient was then treated with two courses (15 + 12 injections) of diamidino-stilbene and was completely cured of kala-azar. He was seen more than six months after the completion of the treatment for kala-azar and was in excellent health except for the fact that he had developed 'Diamidino-stilbene Neuropathy'.

Case 2.—M. T. I., an Indian male child, aged 3 years 4 months, was admitted on 21st April, 1944, for irregular attacks of fever at intervals of about two weeks since July 1943 and diarrhoea with passage of mucus streaked with blood for two days. The child was thin, anæmic and asthenic. The spleen was enlarged up to 2 inches below the tip of the 9th left costal cartilage, and the liver ½ inch below the costal margin. The patient was afebrile. With symptomatic treatment the diarrhoeic condition subsided. On the 1st May, 1944,

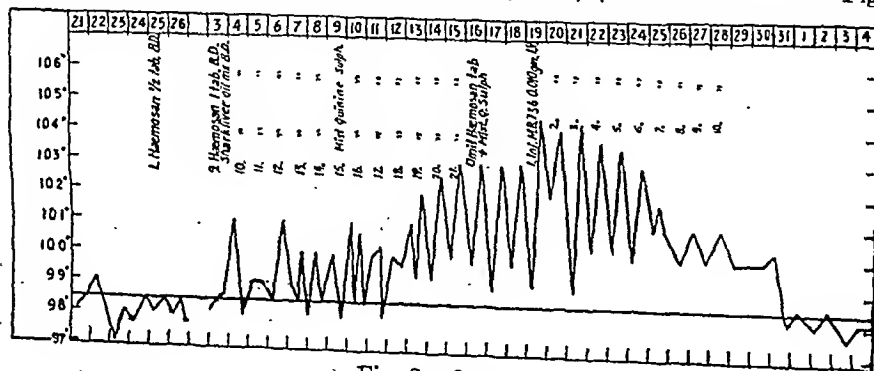


Fig. 2.—Case 2.

the patient commenced to have fever, remittent in type. The temperature increased progressively in the course of the next few days. On the 1st May, *P. vivax* schizonts were found in the peripheral blood film, but

none at all on the days following till the 9th May, when the parasites again appeared, in spite of the fact that no treatment was prescribed during this period. From the 9th to the 11th *P. vivax* ring forms were found. The patient was put on quinine, but this had no effect on the fever which went on rising up to progressively higher degrees of temperature. The complement-fixation test for kala-azar was done on the 8th May, 1944, and was found to be positive. A sternal puncture was done at the end of the seven days' course of quinine and *Leishmania donovani* was found. The patient was then put on specific treatment for kala-azar (see figure 2).

## II. Cases showing malarial infection during the course of treatment of kala-azar with—antimony compounds

Case 3.—P. J., an Indian male, aged 20 years, was admitted for kala-azar on 5th October, 1943. The patient had been suffering for four months. The onset was 'enteric-like'. The patient was weak and anæmic, and there was oedema about the ankles. The spleen was enlarged up to 6 inches and the liver 1½ inches. *Leishmania donovani* was found in the sternal puncture smear, and the patient was put on a course of aminostiburea, the injections being given on alternate days. The fever began to fall after the third injection, and the patient was afebrile from the day after the eighth injection. On the day following the 11th injection, the patient had a sharp attack of fever in the afternoon, the temperature rising up to 101°F. No malarial parasites were found in the blood film examined on this day. The fever gradually subsided by 10 o'clock next morning, and the patient had the 12th injection as usual. On the next day, the patient had another attack of fever, this time with chill and rigor, and the temperature rose up to 105°F. (see figure 3). On examination of blood film, *P. vivax* ring forms were found. The patient was put on

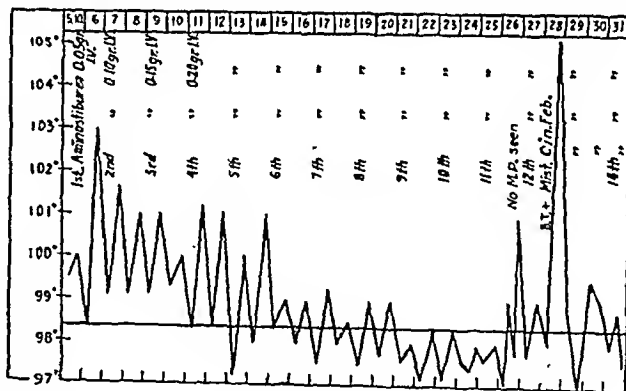


Fig. 3.—Case 3.

cinchona febrifuge to which he responded readily. The treatment for kala-azar was not interrupted, and the patient made an uneventful recovery.

Case 4.—H. S., a Jewish girl, aged 15 years, attended the kala-azar outpatients' clinic on the 14th February, 1944, for attacks of fever since December 1943. The onset was enteric-like, remittent pyrexia lasting about three weeks. This was followed by a short period of pyrexia and then there was a relapse of irregular type of pyrexia. The patient was thin and anæmic; splenic enlargement 4 inches and the hepatic enlargement up to 1 inch below costal margin. *Leishmania donovani* was found

there was a relapse of irregular type of pyrexia. The patient was thin and anæmic; splenic enlargement 4 inches and the hepatic enlargement up to 1 inch below costal margin. *Leishmania donovani* was found

on sternal puncture and the patient was put on injections of aminostiburea, twice a week. The patient became afebrile after three injections. The treatment was interrupted for 12 days from 8th March, 1944, to 20th March, 1944, on account of the patient developing otitis media. The treatment was continued regularly after this break. She had the 15th injection on 27th April, 1944. On 3rd May, 1944, afternoon she had an attack of fever with slight chill and headache and the temperature went up to 104°F. The next day the temperature ranged about 100°F. On the 5th May, she had another attack of high fever without any actual rigor; only slight chill was felt. Blood film was examined for malarial parasites but none was found on this date. The patient was advised admission into the hospital and till she was admitted on 11th May, 1944, she continued to have fever on alternate days. On 11th May, 1944, blood examination revealed *P. vivax* ring forms and growing trophozoites. The patient was put on a course of quinine and the fever rapidly subsided. The spleen which measured 3 inches on the 11th May, rapidly decreased in size and was barely palpable at the end of the course of quinine. She did not require any further treatment for kala-azar and made an uninterrupted recovery.

**Case 5.**—The temperature chart of one other hospital case is reproduced from a publication by Napier (see figure 4). This patient showed benign tertian malarial infection towards the end of a course of antimony injections. It will be seen that the fever gradually came down almost to normal during the course of

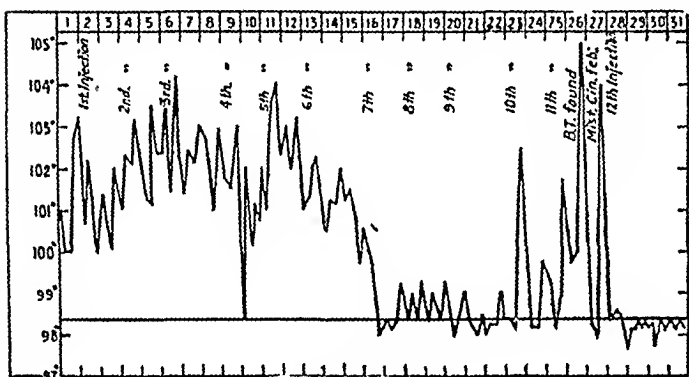


Fig. 4.—Case 5.

treatment but the residual temperature after the 8th injection suggested malaria. Even on the day of the 10th injection when the patient had a high rise of temperature no malarial parasites were found. Only when the patient had a rigor subsequent to the 11th injection were the benign tertian malarial parasites found. The fever responded immediately to cinchona febrifuge.

### Discussion

The above five case reports illustrate the clinical features of malarial infection complicating kala-azar. In all, with the possible exception of case 4 where a subsequent infection with malaria cannot be ruled out, the malarial infection was co-existent with the leishmanial infection.

In the first group of cases, the parasites were detected during the febrile stage of kala-azar previous to any specific anti-kala-azar treatment. It will be seen that in these cases very small numbers of parasites could be found in the peripheral circulation, and the pyrexia that was present was obviously not due to malarial infection. The fever remained entirely unaffected in spite of the fact that the patients were given adequate doses of quinine and the malarial

parasites had disappeared from the peripheral blood as a result of quinine. Also the pyrexia present when the malarial parasites were found had no similarity to a characteristic malarial paroxysm. It is likely that in these cases the multiplication of the malarial parasites was held in check, possibly as a result of the concurrent active leishmanial infection, and the number of parasites in the blood stream was so small that no malarial paroxysm could be caused.

In the second group of cases (cases 3, 4 and 5) the malarial infection became manifest towards the end of the course of treatment for kala-azar. The fever was not very typical of malaria in the first few paroxysms, and though the temperature rose quite high, no malarial parasites could be found in thin blood films in the first few bouts of fever. Later, the paroxysms became typical of malarial fever, and the parasites were found. In these cases, it appears that multiplication of malarial parasites could take place only when the leishmanial infection was controlled, and the number of parasites sufficient to cause a malarial paroxysm could develop. The infection was readily eradicated by cinchona alkaloids. The splenic enlargement also rapidly subsided after the course of cinchona alkaloids.

In this connection, it may be mentioned that it is common experience that, even after a course of treatment of kala-azar, sometimes there is a little residual pyrexia, or/and the diminution of the size of the spleen is not as can be expected in uncomplicated cases. In such cases, a course of cinchona alkaloids is found to cause a disappearance of fever and diminution of the size of the spleen, though no malarial parasites may be found in the peripheral blood. It is likely that in such cases malarial infection causes the slight pyrexia and persistence of splenic enlargement.

### *Do the antimonials used in the treatment of kala-azar have any antimalarial action?*

Schmidt and Peter (1938) have discussed this question very thoroughly. The consensus of opinion seems to be that the antimonials have no action on the asexual forms of the malarial parasite. That tartar emetic had no direct antimalarial action was realized quite early (Rasheed, 1923). Other trivalent and pentavalent antimonials tried in the treatment of malaria with similar results were antimosan, stibenyl and stibosan. This finding is further corroborated in cases 3, 4 and 5. In these cases, malarial infection was not checked nor were the malarial pyrexia attacks controlled in any way by the pentavalent antimony compounds given in full doses, both previous to and during the attacks of malarial fever.

The injections of antimonials are regarded as being capable of provoking a malarial attack (Schmidt and Peter, *loc. cit.*). Napier (1927) had found that towards the end of a course of treatment for kala-azar, malarial fever might

occur. Peter was able to make a similar observation in bilharzia patients treated with antimosan. These two observations are however capable of an alternative explanation. It is quite possible that during the stage of active infection with leishmania or even bilharzia, the malarial infection is held in check so that the malarial parasites cannot multiply sufficiently to cause a paroxysm of fever. Napier *et al.* (1933) attributed this to the histiocytosis present in kala-azar. Histiocytes could check the malarial infection, but when as a result of anti-kala-azar treatment these cells disappeared, malarial infection became clinically apparent.

On the other hand, Fischer found that, in several cases of chronic malaria which showed only crescents in the peripheral blood, stibenyol caused the occurrence of clinical attacks accompanied by the reappearance of the ring forms. Nunno found that intravenous injections of tartar emetic produced considerable irritation of the elements of the reticulo-endothelial system, and produced a real mobilization of malarial parasites, both trophozoites and crescents, and more or less typical attacks occurred. Also he observed a cure in a number of chronic malarial cases.

If as is Fischer and Nunno report, antimony injections may activate a latent malarial infection, then the question arises whether antimony might be given to patients after quinine treatment as a test of cure, the return of the parasites and fever indicating the necessity for further specific treatment.

#### Summary

1. Malarial infection may complicate kala-azar before and during treatment with pentavalent antimony compounds. In the few untreated cases of kala-azar that show malarial parasites in the peripheral blood, the number of parasites is usually small, and it has been found that the fever is not due to the malarial parasites. In cases where there is malarial pyrexia towards the end of the course of treatment (by pentavalent antimonials) of kala-azar, the pyrexia is due to malarial parasites. In these cases, the co-existing malarial infection remains latent as long as the leishmanial infection is not controlled by the specific treatment with antimonials, and only when kala-azar has been controlled can the malarial parasites multiply sufficiently to cause a malarial paroxysm.

2. The pentavalent antimony compounds have neither a preventive nor a direct curative action on the malarial parasites.

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## NUTRITIONAL MACROCYTIC ANÆMIA AMONGST VEGETARIANS IN FORWARD AREAS IN THE MIDDLE EAST CAMPAIGN\*

By BALBIR SINGH

CAPTAIN, I.A.M.C.

THIS subject has been reviewed by Trowell (1943) in a recent article in the *Lancet*. We had the opportunity to investigate a few cases on field service overseas. Barber has recorded investigations of 18 cases in the Middle East (personal communication). Walter has recorded 23 cases in a general hospital in Persia and Iraq Force (personal communication).

We will discuss in this paper 5 cases whose records are available to me.

**Case 1.**—Havildar, Rajput, resident of Gurgaon, vegetarian; service 9 years; had been overseas for 2½ years. Admitted on 24th October, 1942. Felt feverish at Cairo when he was on his way to Persia and Iraq Force. Did not feel fit during the journey. Felt very weak when he reached Boom Town.†

Complained of breathlessness, weakness, puffiness of the eyes and nervousness.

**Physical examination.**—Liver and spleen not palpable, heart sounds normal, no murmur.

**Laboratory investigation.**—Urine—albumin a trace; stools—no ova detected by concentration method on three examinations; van den Bergh negative; malarial parasite—negative; megaloblast—nil; normoblast—intermediate and late types present; size of red blood corpuscles—7.8μ.

**Case 2.**—Havildar, Rajput, resident of Gurgaon, vegetarian; service 9 years; had been overseas for 2½ years. Admitted on 10th November, 1942; had nausea and retching for a fortnight when he was at Cairo 2 months before admission. He complained of breathlessness on slight exertion, feeling of fatigue in knees on exertion, throbbing in the head and loss of appetite.

**Physical examination.**—Liver and spleen—not palpable; heart—pulmonary second sound accentuated; no murmur; lungs—no abnormality.

**Laboratory investigation.**—Stools—no ova detected by concentration method on three examinations; Kohn—negative; van den Bergh—negative; malaria parasite—negative; megaloblast—nil; size of R.B.C.—7.5μ; total W.B.C.—4,800 per c.mm.; polymorphonuclears—67 per cent; lymphocytes—29 per cent; monocytes—2 per cent; eosinophils—2 per cent; normoblasts—present.

**Case 3.**—L/Nk., Rajput, resident of Gurgaon, vegetarian; service 10 years; had been overseas for 2½ years. Admitted to a hospital from 5th October, 1941 to 16th October, 1941, with a diagnosis of secondary anaemia. Again admitted to hospital in Paj Force on 13th January, 1943. He complained of loss of appetite, breathlessness, giddiness and discomfort in the epigastrium on exertion.

**General examination.**—No glossitis or ocular manifestations detected. He was very nervous and emotional. Liver and spleen—not palpable; heart sounds—pulmonary second sound accentuated; urine—

\* This report was written when the writer was working as a pathologist in Persia and Iraq Force.

† Boom Town is a fictitious name for the place where the writer was posted as a pathologist.

CASE 1					
Date	R.B.C. per c.mm.	Hæmoglobin percentage	C.I.	Reticulocytes percentage	Urine albumin
28-10-42	Put on iron 30 grains three times a day and acid hydrochloric dil. Mx.				
28-10-42					
10-11-42	1,550,000	38	1.2	4	a trace
10-11-42	1,770,000	40	1.2	3	a trace
25-11-42	500 c.cm. of whole blood transfused.	56		5	a faint trace
26-11-42	2,800,000				
30-11-42	One ounce of liver extract three times a day as it was available by then.				
30-11-42	Liver extract stopped.				
4-12-42	3,250,000	75	1.0	10	nil
	4,350,000	85	1.0	8	

CASE 2						
Date	R.B.C. per c.mm.	Hæmoglobin percentage (Sahli)	C.I.	Reticulocytes percentage	Normoblasts	Urine albumin
11-11-42	Put on iron tonic mixture (30 grains of iron three times a day) and acid hydrochloric dil. Mx					
11-11-42						
	1,750,000	35	1	4		a trace
24-11-42	1,800,000	37	1	5	late type	a trace
27-11-42	450 c.cm. of fresh blood transfused.	70	1	nil	a few present	nil
6-12-42	3,450,000	85	..	2	nil	nil
12-12-42	4,500,000					

CASE 3						
Date	R.B.C. per c.mm.	Hæmoglobin percentage (Sahli)	C.I.	W.B.C. per c.mm.	Reticulocytes percentage	Urine albumin
18-1-43	1,400,000	28	1.0			
21-1-43	Put on liver extract by mouth.					
25-1-43						
30-1-43	1,670,000	38	1.1	3,125	6	a trace
	2,700,000	60	1.1	..	12	a trace
5-2-43	Liver extract stopped (no longer available).		1.0	..	13	a trace
11-2-43	3,000,000	63	1.0	..	10	a faint trace
17-2-43	3,760,000	71	1.0	..	10	a faint trace
22-2-43	3,980,000	82	1.0	4,800	3	nil
27-2-43	4,480,000	80	0.9	5,200	..	nil
	5,000,000	92	0.9	..	..	nil

CASE 4					
Date	R.B.C. per c.mm.	Hæmoglobin percentage (Sahli)	C.I.	Reticulocytes percentage	Urine albumin
21-1-43	1,450,000	30	1.0		
25-1-43	Put on liver extract by mouth one ounce thrice daily.				
1-2-43					
2-2-43	1,750,000	37	1.1	4	a trace
6-2-43	Liver extract stopped.				
17-2-43	2,060,000	38	0.9	10	a trace
22-2-43	2,070,000	52	0.9	8	a trace
23-2-43	2,710,000	50	0.9	5	a trace
5-3-43	Liver extract one ounce thrice daily.	60	0.8	4	a trace
10-3-43	3,500,000	56	0.8	4	a faint trace
11-3-43	3,750,000	59	..	2	nil
15-3-43	Ascorbic acid 300 mg. daily.	65	0.7	..	nil
20-3-43	3,750,000	66	..	..	nil
25-3-43	4,000,000	68	..	..	nil
30-3-43	4,180,000	66	..	..	nil
4-4-43	4,700,000	68	..	..	nil
7-4-43	Put on iron mixture (30 grains three times a day).	68	..	..	nil
	4,800,000				

## CASE 5

Date	R.B.C. per c.mm.	Hæmoglobin percentage (Sahli)	C.I.	W.B.C. per c.mm.	Reticulocytes percentage	Urine albumin
26-1-43	1,600,000	32	1.0	5,000	3	a trace
30-1-43	Put on milk 5 pounds.					
1-2-43	1,650,000	40	1.2	..	2	a trace
6-2-43	1,780,000	42	1.2	..	..	a trace
7-2-43	Liver injection.					
11-2-43	1,800,000	42	1.1	..	10	a trace
14-2-43	Liver extract stopped.					
16-2-43	2,300,000	55	1.1	..	11	a faint trace
22-2-43	3,180,000	59	0.9	..	8	a faint trace
27-2-43	3,350,000	65	0.9	5,600	3	a faint trace
1-3-43	Ascorbic acid 300 mg. daily.					
5-3-43	3,350,000	67	1.0	..	0.5	nil
10-3-43	4,150,000	76	0.9	..	0.3	nil
20-3-43	4,700,000	84	0.9	..	0.3	nil
25-3-43	5,030,000	98	0.9	..	0.3	nil

albumin a trace; stools—no ova detected by concentration method on three examinations; van den Bergh—negative; Kahn—negative; malaria parasites—negative; free HCl—present; megaloblasts—present; size of R.B.C.—7.7 $\mu$ ; normoblasts—present.

Case 4.—Sowar, B., Jat, resident of district Rohtak; vegetarian; service 5½ years; overseas for the last 2½ years; had three attacks of diarrhoea each lasting for a week. Felt weak for the first time at Cairo where he stayed for 1½ months before coming to Persia and Iraq Force. His condition gradually became worse. Admitted to a general hospital in Paf Force on 18th January, 1943.

He complained of breathlessness and giddiness on exertion, aching of knees, loss of appetite, discomfort in the hypogastrium more marked on exertion, irritability and retching in the morning on getting out of bed.

General examination.—No glossitis, angular stomatitis or ocular manifestations detected. Pulse rate 90 per minute, easily compressible. Liver and spleen—not palpable; heart sounds—pulmonary second sound accentuated. No murmur.

Laboratory investigation.—Urine albumin—a trace; stools—no ova detected by concentration method on three examinations; van den Bergh—negative; malarial parasites—negative; free HCl—present; megaloblasts—nil; normoblasts—primitive, late and intermediate forms—present; size of R.B.C.—7.6 $\mu$ ; total W.B.C.—5,600 per c.mm.; polymorphonuclears—42 per cent; lymphocytes—54 per cent; monocytes—2 per cent; eosinophils—2 per cent.

Case 5.—Sowar, Jat, vegetarian and resident of district Hissar, service 1½ years; overseas 5 months. Admitted with the complaints mentioned below. Duration one month.

Complaints were breathlessness and giddiness on exertion, feeling of fatigue after exertion, irritability and loss of appetite.

General examination.—No glossitis or angular stomatitis, pallor marked. Liver—not palpable; spleen—palpable; heart sounds—pulmonary second sound accentuated.

Laboratory investigations.—Urine—albumin a trace; stools—no ova detected by concentration method on three examinations; Kahn—negative; van den Bergh—negative; malarial parasites—negative; free HCl—present; megaloblasts—nil; normoblasts—a few, late type; size of R.B.C.—7.6 $\mu$ .

The medical officer of the unit informed me that the incidence of diarrhoea and boils was higher amongst the vegetarians than in the non-vegetarians. He was of the opinion that the vegetarians made remarkable improvement in their health during their stay of 4 months in Boom Town. He referred to 2 cases with similar complaints that he observed before the units reached Boom Town. One of them was repatriated to India. Details of the other findings available for my examination are given below:—

Examination of four men from the unit.—These men were sent by the medical officer for investigation as they complained of breathlessness on ordinary exertion. An attempt was made to obtain more evidence from the units. This part of the investigation was not fruitful because of the movement of the units to a different station.

These men were Jats, vegetarians, and belonged to Rohtak except no. 1, who was a Rajput and came from Aligarh.

No. 1. Low colour index and eosinophilia suggest secondary anaemia due to worm infection. Stools could not be examined.

No. 2. No conclusion could be drawn from this case.

No. 3. He had R.B.C. 3,750,000 per c.mm.; hæmoglobin (Sahli) 75; C.I. 1; no eosinophilia, gradually progressing weakness for the last 6

## DETAILS OF FOUR CASES

Number	Name	R.B.C. per c.mm.	Hæmoglobin percentage (Sahli)	C.I.	Eosinophils	Service overseas	Total service in years
1	B.S.	3,250,000	48				
2	C.	3,770,000	80	0.7	12	10	1½
3	C.B.	3,500,000	75	1.0	4	10	1½
4	M.S.	3,600,000	75	1.0	2	33	6
						30	7



months; overseas for the last  $2\frac{1}{2}$  years; total service 7 years; vegetarian; resident of Rohtak and no history of dysentery or malaria. The history as well as the blood counts of this case closely resembled the 5 cases already described. He appeared to be at an early stage of the syndrome observed in them.

No. 4. M. S., unit A; Sowar, Jat, vegetarian and resident of Rohtak; service 7 years; had been overseas  $2\frac{1}{2}$  years. First noticed weakness 4 months ago. Complained of breathlessness on exertion, inability to work, and weakness of vision 20 days after he felt weak. Had no glossitis or stomatitis. Admitted to a C.C.S. for two weeks, to a general hospital for three weeks and to another for  $1\frac{1}{2}$  months. His complaint resembled those of the 5 cases described above. This man was treated for 4 months but his blood counts did not reach a satisfactory level, and he did not feel fit. I think he could not make a complete recovery as he was not treated for deficiency of the extrinsic factor.

#### Discussion

*Symptoms.*—The symptoms in these cases were: (i) breathlessness and feeling of fatigue on slight exertion; (ii) weakness; (iii) loss of appetite; (iv) throbbing in the head; (v) nervousness; (vi) discomfort in the epigastrium or hypogastrium on exertion; (vii) weakness of vision, complained by two of them. Glossitis, angular stomatitis, cheilosis and ocular manifestations characteristic of riboflavin deficiency were absent. No conclusion could be drawn from the symptoms with regard to the aetiology of the syndrome. They may be present in anaemia due to any cause.

*Laboratory findings.*—Salient features were: C.I. varied from 0.9 to 1.2, size of the R.B.C.  $7.5$  to  $7.8\mu$ , reticulocytes 3 to 6 per cent, megaloblasts absent, normoblasts of the intermediate and late type present, free HCl present in three of them in whom it was examined. Kahn negative, no malarial parasites detected in blood films, no ova of worms in stools.

This investigation showed that these cases were suffering from macrocytic anaemia.

The absence of megaloblasts, the presence of free HCl and the van den Bergh test ruled out pernicious or Addisonian anaemia. The syndrome of macrocytic anaemia results from a variety of causes. Syphilis, malaria, and worm infection were excluded by the laboratory investigation.

*History.*—Important factors were: (i) all these cases were vegetarians and belonged to Rohtak, Hissar, or Gurgaon district. Cases recorded by Barber and Walter came from the same communities; (ii) fresh milk and ghee prepared at their home were important sources of vitamins in their diet in peace time. Dried or evaporated milk in lieu of fresh milk and ghee from the stores were supplied on active service; (iii) 3 cases belonged to one unit, and 2 to another; (iv) non-vegetarians from the same units showed no case of this type.

Factors 1, 2 and 4 suggest that dietary may have something to do with the development of the syndrome of macrocytic anaemia. Why should not the vegetarians from other units show similar cases?

There were two additional factors, viz (i) service in the forward areas for two years, (ii) constitutional factors.

These men belonged to special communities of the three above-mentioned districts of Punjab which are famous for their famines. Repeated famines and the poor nutritive condition of the inhabitants may have produced some inherent defect in their constitution.

*Dietary.*—It is not within the scope of this paper to assess the vitamin-nutrition of the ration of these people; nor is it of much use in discussing the aetiology of macrocytic anaemia, as the exact nature of the haematinic factor or Castle's extrinsic factor is still unknown. I have however mentioned the important differences in the dietary of these people in India and on service overseas. It may not be out of place to mention that Kon (1941), in a recent article in *Nature* on the nutritive value of different forms of milk, stated in reference to the unsweetened evaporated milk, which is used by these people very often, that there is a slight decrease of protein value, 60 per cent loss of vitamin C and a 30 to 50 per cent loss of B<sub>1</sub>. Loss of vitamins is much less from sweetened condensed milk of good quality, but the medical officer informed me that they preferred the former. Muthanna and Seshan (1941) reported in the *Indian Medical Gazette* the gross deterioration that takes place in the vitamin A content of the ghee by a storage or exposure to light.

*Information supplied by the medical officer of Unit A.*—(a) They had two similar cases amongst the vegetarians before this unit reached Persia and Iraq Force.

(b) The health of the vegetarians was poorer than that of the non-vegetarians.

(c) The vegetarians made remarkable improvement in their health during their stay of four months in Boom Town.

The medical officer's information based on personal observation, but without any record could be considered as an opinion only, but as the medical officer had been with the unit for more than  $1\frac{1}{2}$  years, I should consider that this opinion is suggestive of some factor handicapping the vegetarians. His observation that the vegetarians in the unit made remarkable improvement during their stay in Boom Town could be due to reduced requirements of the body metabolism. Spies *et al.* (1940) reported that rest is sometimes able to cure even specific lesions caused by deficiency in dietary.

*Treatment.*—Important factors were: (i) 2 cases did not react to iron, 30 grains thrice daily, for a fortnight. They improved on blood transfusion (1 pint only); (ii) the other three were amenable to liver therapy.

Unfortunately the cases were so few that no controls for comparison were available. It cannot be stated from the facts available that none of them reacted to iron. Captain Barber who was in charge of the last 3 cases did not put them on iron in view of his previous experience of a few similar cases in the Middle East. The first two cases were treated with blood transfusion because liver extract was not available; it cannot be stated whether they could have improved on liver as it was never given a trial; nor they could be classed as pseudoplastic.

The last three cases reacted to liver therapy. It could be concluded that there was deficiency of hæmatinic factor; unfortunately the nature of these factors is still a puzzle to the physiologists. No conclusion can be based on the information available from treatment.

*Relative incidence amongst the regulars and recent recruits.*—Three out of the five had 10 years' service, one 5½ years and the other 1½ years only. Four out of these five had more than 2 years' service overseas.

*Age incidence.*—The incidence of pernicious anæmia increases with age. I do not think the higher incidence of macrocytic anæmia amongst the regulars could be associated with older age.

The number of cases is far too small to satisfy a statistician, but the whole data presented in this report suggests that it is not improbable, although it can be disputed, that anæmia in these men resulted from a state of dietary deficiency. Whether it was a protein deficiency or hypovitaminosis can be established by further work only.

#### Summary

1. Five cases of macrocytic anæmia amongst vegetarians in the Indian Army are described.
2. The evidence available is suggestive of a deficiency in dietary.

#### Acknowledgments

My thanks are due to officer commanding of the General Hospital and colleagues in the medical section for providing me facilities to investigate their cases. Thanks are also due to Subedar K. S. Ramaswami, I.M.D., who helped in the investigation of these cases.

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### GHEE AS A SOURCE OF VITAMIN A IN INDIAN DIETARIES: THE EFFECT OF COOKING ON THE VITAMIN CONTENT OF FOODS

By G. KARMAKAR

(From the Department of Biochemistry, Nutrition and Physiological Hygiene, All-India Institute of Hygiene and Public Health, Calcutta)

*The place of ghee in Indian dietaries.*—Ghee forms one of the chief sources of vitamin A in

the diet of Indians and specially of vegetarians. It is consumed as ghee and in fried preparations such as puri, fried fish, meat cutlet, vegetable curry, mutton curry and sweetmeats. There is a considerable variation in the vitamin A content of butter and ghee prepared from the milk of cows in different parts of India.

*Quantity of ghee consumed in different provinces of India.*—The diet surveys in different provinces of India are not yet complete. The data obtained so far provide some information on the consumption of ghee in different parts of India. These figures refer apparently to raw ghee and not to ghee in the cooked form.

From table 1 we have an idea of the quantity of vitamin A available from the Indian dietaries. The highest recorded amount of ghee consumed is 2.0 oz. (D. D. Mitra, 1939). The highest value of vitamin A in ghee so far recorded is 55 I.U. per gramme (Muthanna and Desnan, 1941). On this basis, 3,000 I.U. of vitamin A is consumed in 2 ounces of ghee. This however is only approximately the minimum daily requirements. It is also obvious that in the majority of the provinces the consumption is below 1 oz., making vitamin A consumption less than half of the minimum requirements. This amount is made still lower if ghee with a lower vitamin A content such as 15 I.U. (Muthanna and Desnan, *loc. cit.*), or even if the average type of ghee with 20 to 25 I.U. is consumed.

*Effect of heating.*—Many workers have recorded loss of vitamin A in ghee on heating. It has been shown that heat in the presence of air, aeration and hyalogenation is destructive to vitamin A (Grewar, 1933; Drummond, Channon and Coward, 1925). Banerjee and Doctor (1938) studied the loss of vitamin A in ghee due to exposure, irradiation and auto-oxidation. It has also been reported that vitamin A is destroyed in milk as a result of boiling (Decaro and Speier, 1935).

*Effect of cooking.*—Little information is available with regard to loss of vitamin A in ghee as a result of its use for cooking. In order to elucidate this point, it was thought worth while to carry out experiments on the estimation of vitamin A in the (1) original ghee, (2) ghee left over after cooking and (3) ghee extracted from the cooked food. Almost all the methods of cooking done with ghee were employed.

*Preparation of puri and other articles:* Puri.—Atta was mixed with a requisite amount of water and ghee and kneaded into a uniform dough of proper consistency. Portions of that dough were rolled into circles of uniform thickness and fried in ghee. The ghee was first heated for about 3 minutes and the frying was continued from 12 to 15 minutes at a temperature between 200°C. and 250°C. The average weight of each puri thus prepared was about 20 gm. Three such puris were then cut into small pieces and dried in a vacuum desiccator overnight. Then they were placed within an extraction thimble and the ghee was extracted with freshly distilled ether in a Soxhlet five or six times. The ether was evaporated and the ghee obtained from the three puris was about 10 gm. Its vitamin A content was estimated.

TABLE I  
Consumption of ghee in different provinces

Province	Distriet	Population	Quantity per consumption unit per day, oz.	Surveyed by
Madras ..	Mayanur and Chingleput.	Rural	Only 3 families out of 44 found to consume ghee 0.5 to 0.9	Aykroyd and Krishnan (1937).
Mysore ..	Mysore	Do.	0.1	
Orissa ..	Puri	Urban	0.2	Singh (1939).
C. P. and Berar	Nagpur	Rural (poor class)	0.14	Bhave (1941).
	Tirodi	Do.	0.3	Do.
	Warud	Rural	Nil	Do.
Bengal ..	Calcutta	Urban (well-to-do)	2.0	D. D. Mitra (1939).
Bihar ..	Jamshedpur	Urban	0.5 to 1.8 (ghee and vegetable oil).	K. Mitra (1940).
Delhi ..	Najafgarh	Rural	0.5	Shourie (1939).
		Semi-urban	0.3	Do.
U. P. ..	Narendranagar	Rural	0.4	
Punjab ..	Ferozepore	Rural	1.2	Ahmad and Gore (1938).
		Urban (middle class)	1.5	Do.
		Sweepers	0.4	Do.
Hyderabad ..	Nizamabad	Small agriculturists.	0.08 to 0.16	Daver and Ahmed (1942).
		Depending on agriculture only.	0.2 to 0.4	Do.
Coorg ..	Mereara Town	Urban	0.1 (Ghee + butter)	Bhave and Bopaiya (1942).
	Villages near to Mereara Town.	Rural	Nil	Do.
Bombay ..	Bombay City	Urban (middle class)	0.7	Niyogi and Sukhatankar (1939).
		Sweepers	Nil	Do.

**Brinjal, potato chip and fish.**—Chips of brinjal, potato and fish were coated with a paste made up of dal, flour, salt and spices and were fried in fresh quantities of ghee in each case. The temperature during the process of frying was between 200°C. and 220°C. and it was continued for 8 to 10 minutes. The fried articles were then dried in a vacuum desiccator and ghee was extracted in a soxhlet as described above. Its vitamin A content was estimated.

**Mutton cutlet.**—Mutton was chopped into pieces and then coated with egg white mixed with bread crumbs. The raw cutlets were then fried in ghee for 5 minutes at a temperature of about 200°C. Ghee was then extracted from the fried cutlets, and its vitamin A content was estimated.

**Mutton curry and vegetable curry.**—A few sliced onions were fried in some ghee at about 200°C. Then some pieces of mutton were spiced with the fried sliced onion and cooked for 16 minutes as usual. The temperature during cooking ranged from 95°C. to 99°C.

In a similar manner vegetable curry was prepared with lady's finger, cauliflower, potato, etc. and the temperature during cooking was about 97°C.

In the case of curry, the solid materials were ground in a mortar and the whole mass was diluted with water. The solution was then extracted with distilled ether. The ether solutions were orange-coloured in the case of both the curries, and so they were shaken for a minute or two with *norite* charcoal just sufficient to remove the pigments only. The ether being evaporated, ghee was obtained.

**Sweetmeat (lady-canning and chanar jilipi).**—Small balls of chana (chana mixed with requisite amount of flour) were prepared and fried in ghee for 11 to 12 minutes. The temperature of frying was between 140°C. to 160°C. The fried balls were then dipped into hot dilute sugar solution, which are popularly called 'lady-cannings'. In this way, three lots of lady-canning were prepared.

Another variety of sweetmeat of different shape called 'chanar jilipi' was prepared in a similar manner but

the frying was continued for a lesser period, say 7 to 8 minutes. After frying they were dipped into the same sugar solution which was finally heated for 6 minutes at 93°C.

The lady-canning and chanar jilipi were separately ground in a mortar, diluted with water and extracted with ether. The ether solution was then evaporated to dryness to obtain the fat.

The original 'chana' had been examined before and found to contain no vitamin A.

**Method of estimation of vitamin A.**—The spectrophotometric method was employed for vitamin A determination.

About 5 to 10 grammes of ghee were saponified and the non-saponifiable fraction was dissolved in about 10 c.cm. cyclohexane. The quartz cell was then filled with this solution and the compensating cell with the solvent. A series of exposures were given by gradually reducing the aperture of the rotating sector and the spectra were photographed in a medium-size quartz spectrograph. The extinction coefficient of a 1 per cent solution in 1 cm. cell at 328 mμ was determined from the photograph. This value of the extinction coefficient multiplied by the factor 1,600 gives the potency of vitamin A in International Units.

The potency of vitamin A was also determined by the colorimetric method for comparison.

In this method the blue colour produced by the action of saturated solution of SbCl<sub>5</sub> in chloroform on a certain known volume (0.2 c.cm.) of the non-saponifiable fraction of ghee in chloroform was matched with the standard blue-coloured glasses in the Lovibond tintometer. The blue units were then multiplied by the conversion factor (which is about 50 for a 20 per cent solution in a 1 cm. cell) for obtaining the potency in International Units.

TABLE II  
*Frying of puri, etc., in ghee*

Name of fried articles	Temperature of cooking, °C.	Duration of cooking, min.	Weight of the cooked articles, gm.	Quantity of ghee extracted, gm.	Quantity of ghee from 100 gm. of food, gm.
Puri ..	200-250	12-15	60	10	16.6
Brinjal ..	200-220	8-10	60	9	15.0
Potato chip ..	200-220	8-10	45	7	15.5
Fish ..	200-220	8-10	55	8	14.5
Mutton cutlet ..	180-200	6	83	12	14.5
Mutton curry ..	{ 200 98	1½ } 17½	95	11	11.6
Vegetable curry	{ 200 97	1½ } 10½	102	8	7.8
<i>Sweets :</i> <i>Lady-canning</i> ..	140-160	11 for each lot.	90 with sugar solution.	10	11.0
<i>Chanar jilipi</i> ..	140-160	8	80 with sugar solution.	8	10.0

*Results.*—Table II gives the amount of ghee present in the various cooked foods. Table III gives details of vitamin content of original ghee (3 samples) and of ghee left over after cooking or obtained from the cooked food.

TABLE III

*Effect of frying and cooking on vitamin A content of ghee obtained from a village near Calcutta*

Name of fried or cooked articles	Quality of ghee	POTENCY OF VITAMIN A	
		Spectro-photo-metric method, I.U./gm.	Colori-metric method, I.U./gm.
	Sample I	24	26
Puri ..	Left after frying puri.	Nil	Nil
	Extracted from puri.	Nil	Nil
Brinjal ..	Left after frying brinjal.	4	5
	Extracted from brinjal.	5	Not done
Potato chip	Left after frying potato chips.	5	3
	Extracted from potato chips.	5	Not done
Fish ..	Left after frying fish.	4	5
	Extracted from fried fish.	5	Not done
	Sample II	18	15
Mutton cutlet	Left after frying mutton cutlet.	4	5
	Extracted from mutton cutlet.	3	4
Mutton curry	Extracted from curry.	3	4
Vegetable ..	Extracted from curry.	2	Not done

TABLE III—concl'd.

Name of fried or cooked articles	Quality of ghee	POTENCY OF VITAMIN A	
		Spectro-photo-metric method, I.U./gm.	Colori-metric method, I.U./gm.
	Sample III	25	23
Lady-canning	Extracted from lady-canning.	4	5
	Left after frying the first lot.	11	15
	Left after frying the third lot.	Nil	Nil
Chanar jilipi	Extracted from jilipi.	13	15
	Left after frying jilipi.	17	16

*Discussion.*—At the high temperature of frying, which is above 200°C., most of the vitamin A present in ghee is destroyed, and consequently the ghee extracted from the fried articles is found to be very poor in vitamin A content. Traces of vitamin A detected in fried fish, brinjal, potato chip, and other articles may be due to the fact that the ghee was heated only for a short time. For large-scale preparations as required in families and shops, the heating of ghee is prolonged more than 10 minutes, in which case practically all the vitamin A will probably be destroyed. It would appear that from the dietary survey made so far it will not be possible to assess the real intake of vitamin A by means of estimating the consumption of ghee.

*Summary.*—The highest level of intake of vitamin A through consumption of fresh and genuine ghee never reaches more than the minimum requirement in India. Vitamin A in ghee is destroyed at the high temperature of frying, and the ghee carried along with the fried

articles contain practically no vitamin A. Even with small-scale preparations, however, when ghee is heated for a short while, it is found to contain only 25 per cent or less of the original vitamin A.

### Acknowledgment

Thanks are due to Lieut.-Colonel E. Cotter, C.I.E., I.M.S., Public Health Commissioner with the Government of India, who kindly suggested the investigation, and to the Indian Research Fund Association for financial assistance.

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### ERRATUM

THE following is the description of plate XXII (figures 1 to 16) illustrating the article on 'Developing gametocytes and schizonts of *Plasmodium falciparum* : A case showing all stages in the peripheral circulation', by B. M. Das Gupta and S. K. Ganguli, published in the October issue of the *Gazette* (p. 458) which was, by error, omitted.

Figures 1 to 7 developing crescents, 6 and 7 showing two immature crescents in the same corpuscle.

Figure 8, mature female crescent.

Figure 9, developing schizont.

Figure 10, a schizont and a gametocyte in the same corpuscle.

Figures 11 and 12, mature schizonts phagocytosed by polymorphonuclear leucocytes.

[Figures 1 to 12 drawn with camera lucida to the same magnification.]

Figures 13 and 14, two crescents in the same corpuscle.

In figure 14, the crescents appear as if they are fused together.

Figures 15 and 16, schizonts phagocytosed by polymorphonuclear leucocytes.

[Figures 13 to 16, photomicrographs ( $\times 4000$  approx.).]

Note.—The pigment is scattered in developing crescents but occurs as a compact mass in all stages of asexual development.

## A Mirror of Hospital Practice

### AN UNUSUAL ACCIDENT

By MANORANJAN CHANDA, L.M.F.

Chanda Niketan, Manikganj, Dacca

A boy, aged 11 years, climbed a guava tree to pluck fruit, and he fell on to a bamboo stump,  $6\frac{1}{2}$  feet tall which had been cut off diagonally leaving a sharp end. The bamboo stump pierced the left axilla, came out under the middle part of the left clavicle, then pierced the outer and lower part of the neck on the left side passing behind and tearing the trachea and came out behind the right ear. The boy was hanging on its articulation (see figure). The boy was hanging on the stump in this position for about 15 minutes when

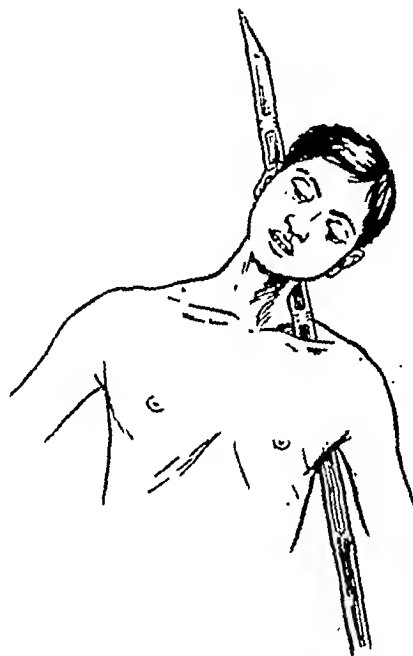
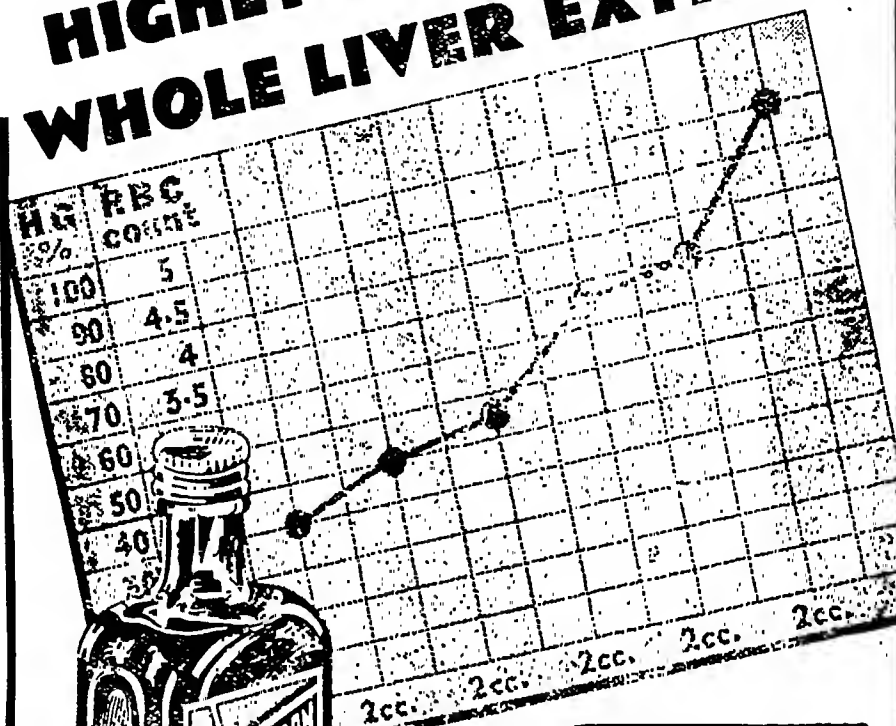


Figure showing the bamboo stump, pierced with its sharp end.

help came. The bamboo stump was broken off, and was then pulled out of the wound. The local doctor stitched the wound and applied bandages, and the patient was then brought ten miles to a hospital in an unconscious state. The bleeding was profuse and shock was marked. Intravenous saline and glucose were administered; the wounds were washed with acriflavin in normal saline and were dusted with sulphanilamide powder. Some bleeding from the nose and mouth continued, and some blood was vomited. That night, the temperature was very high; the pulsating carotid artery was visible through the upper wound. The wound became septic, and some stitches were removed and local treatment was applied.

The patient regained consciousness on the third day and on the fourth day swallowed a little fluid with difficulty but most of it was returned through the nose. Some fragments of bone were removed from the upper part of the wound. For the next two months there was a hectic type of temperature, and at the end of this time about  $\frac{3}{4}$  inch of bone was discharged from the upper wound, and then the fever declined and the wound healed. Apart from some stiffness of the articulation there is no serious disability. About 1½ months after the healing of the wound, an x-ray was taken which revealed no abnormality except some loss of bone from the right mandibulo-maxillary joint.

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# Indian Medical Gazette

NOVEMBER

## TREATMENT IN THE RICKETTSIAL DISEASES

In recent years with such advances in the development of chemotherapeutic agents in the treatment of many diseases, one of the disappointing things has been that so far no chemotherapeutic agent has been discovered which is of undoubted value in the treatment of diseases caused by either viruses or rickettsiae. In some diseases considered to be caused by viruses, chemotherapeutic agents may have some value, but not because of their action on the viruses themselves but because of their action on the secondarily infecting organisms. This is apparently the position with regard to the treatment of trachoma, small-pox and possibly other diseases also. So far, the treatment of virus and rickettsial diseases with drugs of the sulphonamide group has given results which would seem to be of little value.

In virus and rickettsial diseases, the serum of convalescents has been used in treatment but even regarding the value of this measure opinion is divided.

Recently however Andrews and others (*see Lancet*, June 17, 1944) reported the study of a series of compounds for chemotherapeutic action against viruses and rickettsiae, and found one substance V147 (p-sulphamidobenzamidine hydrochloride) which appeared to have an action on the rickettsiae. These authors worked with three strains of rickettsiae of the murine type, and experimented on the action of this drug in experimentally infected mice, and the results appeared very promising. The drug appeared to have a definite action in preventing the development of pulmonary lesions following intranasal inoculation, or else in reducing their size and number, and also prevented death in many cases. The effect was seen when the drug was given before infection, but was still demonstrated if administration was delayed until 42 hours after infection. In typhus-infected guinea-pigs, however, the results of treatment were not satisfactory.

All these results are reported in the paper mentioned above, and they encouraged the hope that these agents might be active in epidemic typhus. Unfortunately however the paper is followed by an addendum briefly reporting a trial of the drug in the outbreak of typhus in Naples. The results were reported to be very disappointing, and it is stated that 'no therapeutic benefit in cases of typhus in man could be shown'. An unexplained toxicity of the drug in occasional patients was experienced, but it is stated that great difficulty was encountered in

instituting treatment in the first few days of the disease. It cannot be said that hope has been abandoned, but apparently no agent so far available has any specific action of value in the treatment of human typhus.

J. L.

## ANTIMONY IN MALARIA

A FEW months ago we refused to publish in this journal an advertisement of an antimony preparation which was said to be a specific remedy for malaria in all forms. This preparation appeared to be an ordinary pentavalent one. In our present number, we publish an article by P. C. Sen Gupta on malaria complicating kala-azar, in which it is recorded that malaria may occur during or immediately after the period when the patient with kala-azar is being treated with pentavalent antimony. This is perhaps sufficient commentary on the value of pentavalent antimony in the treatment of malaria. Previous work on the subject had shown that the effect of antimony on the attacks of malaria was very slight indeed.

J. L.

## THE BRITISH NATIONAL HEALTH SERVICE

In February of this year was published the White Paper on the National Health Service for Great Britain. This is a document of 85 pages. Conditions in India are of course very different from those of Great Britain, and it is feared that the days of the establishment of such a service in this country are probably in the distant future. Nevertheless, we feel that sufficient of our readers will be interested enough in the subject to wish to be familiar with some of the details of the British scheme. The *British Medical Journal* in February of this year published a summary of the White Paper, and we have thought that many of our readers would be interested in reading this summary; we have therefore printed the whole of this summary in our present number.

## DIET AND HEPATITIS

In many parts of India hepatitis and cirrhosis have for many years been common, and the aetiology of this condition has remained obscure. From time to time suggestions have been made that these conditions were associated with poor diet, particularly diet deficient in protein or in protein of good biological value. In a previous number we published an article by Johnson (*I. M. G.*, Vol. LXXVIII, p. 227) who studied cirrhosis of the liver in South India and considered that the evidence pointed to a dietetic factor. Similar findings and similar suggestions have been made regarding similar conditions in other countries, but, in the absence of more direct experimental evidence on the subject, the theory has been regarded as unproved and it must still be regarded as such.

One observation made by the editor in studying the results of the Bengal Famine has been that, after the famine, many of the so-called sick destitutes admitted to hospital for investigation and treatment showed enlargement of the liver and evidence of cirrhosis, and the question arose as to whether this was the direct or indirect result of malnutrition associated with famine.

In our last issue we published in our Current Topics section two items which appeared to bear on this subject. Gilman quoted the well-known fact that cirrhosis of the liver and primary cancer of the liver had often been encountered in South African Negroes. In investigations into the incidence of cancer in Negro workers in gold mines, not less than 90 per cent of cancer were found to be primarily in the liver, whereas primary cancer of the liver is a very rare finding in Europeans. A racial predisposition to liver cancer in dark-skinned people has been suggested, but Gilman thought that the possibility of a dietetic factor should be considered. Working with rats fed on a diet similar to that taken by the South African Negroes, he records a high incidence of changes

in the liver usually in the form of nodular cirrhosis. Also in our last issue we reprinted a letter by Himsworth and Glynn in which they reported that they also, in rats fed on a similar diet, have produced what they prefer to call a nodular hyperplasia of the liver.

In the *Lancet* of April 8, 1944, there appeared an editorial on diet and hepatitis which makes observations on the subject. This editorial is reprinted in our present issue page 561. Also in our present issue is a summary of an article by Stacey on portal cirrhosis in Iraq, in which the influence of a dietetic factor is postulated.

Thus there seems to be gradually accumulating evidence to show that diet may play an important part in the production of hepatic cirrhosis. Many workers, however, appear to think that diet is not the direct cause, but that a diet deficient in protein produces a liver less resistant than normal to the influence of toxins and viruses. Experience in India will certainly point in this direction, and it is highly desirable that those who have facilities and opportunities for doing so should make further studies of this matter in this country.

J. L.

## Special Article

### ORGANIZATION OF TRAUMATIC SURGERY AND REHABILITATION SERVICE IN INDIA

By B. K. SHEOREY, M.B., B.S. (Bom.), F.R.C.S. (Eng.)  
LIEUTENANT-COLONEL, I.M.S.

EVERY week, thousands of civilians in India suffer accidental injury; every week hundreds of fractures and dislocations are sustained, and hundreds of soft-tissue injuries are suffered, including infections of the hand, burns, tendon and nerve injuries. What proportion of these civilian victims will carry to their grave a shortened limb or a crippling deformity?

How can we reduce this number? What facilities are available to ordinary civilians? Have we a trained personnel or suitable and organized institutions where adequate treatment can be given? All these pertinent questions need careful thought and answer.

The experience of surgeons especially expert in the treatment of these injuries, and the results of organized clinics in other countries, prove that in not more than 2 or 3 per cent is permanent disability inevitable. But unfortunately it must be acknowledged that the general standard of traumatic-surgery treatment in India to-day falls far below the standard set by experts, and many hundred victims of trauma will never work again in their original capacity.

*Bone injuries.*—Twenty-five years ago, it was believed that some degree of permanent disability was the inevitable sequel of nearly all fractures. Mal-union and non-union were accepted as unavoidable complications in certain cases, and in many cases even when the anatomical results were good, the 'functional results' were very often poor.

During the last ten to twelve years, the standard of fracture treatment has been rapidly raised. Mal-union and non-union have almost disappeared; the statistics or published records of organized fracture-clinics in the United Kingdom and other countries show that permanent disability can be avoided in over 95 per cent of fractures.

How have we achieved these results? It is mainly due to the modern conception that a fracture is a dual injury, damage to the bone and damage to soft parts, and that, in the treatment of fractures, the bone and soft-part treatments are of equal importance and are often undertaken simultaneously. Formerly, while the bone was being treated in its various stages, viz reduction, fixation, retention till consolidation, nothing was done for the soft parts. The soft-part treatment was withheld until a later stage, and invariably the muscles became wasted and atrophied and the joints stiff on account of disuse.

High standards and results in the treatment of fractures are not achieved and cannot be

achieved by surgical skill alone, but by careful and expert after-treatment, avoiding complications, and constantly supervising the case until function is normal and the patient's confidence is regained. The last is most important. Farquhar Buzzard has rightly remarked that medical practitioners must be alive to the psychological as well as the physical dangers of a patient who has been in an accident; they must take as much care to prevent infection of his mind with insidious morbid ideas as they do to prevent infection of his body with pathological organisms.

If a comparison is drawn between the results secured from the organized fracture-clinics in other countries and the general results secured throughout this country, it will be seen that the results here are far from satisfactory.

One may ask why are they so unsatisfactory? There are many reasons. Chief amongst them are the absence of organized fracture-clinics generally, and the paucity of trained personnel in fracture and orthopaedic work; moreover, in most hospitals in India, the amazing truth is that fractures are still admitted under the nominal charge of surgeons who take little or no interest in such cases, and who willingly delegate them to the care of inexperienced house surgeons or junior medical officers. On discharge from the ward, no further interest is taken in the recovery of the patient, and he is either left to his own devices or is transferred to the care of an entirely different staff in a massage department, if such exists.

If figures are collected from various hospitals in India, I am sure they will show (except in hospitals where there is a higher standard of treatment and organization, and these can be counted on the fingers) that there is a wastage of many working hours, nay years, and thousands of rupees in compensation, that there is loss of wages which could be avoided, and it is high time that we should set about putting things right. The problem, therefore, is that of the prevention of prolonged disability, as well as permanent disability. Such a state of affairs in its social aspect is a tragedy to the individual and to his family; in its economic aspect it is a tragedy to the community, for the cost must be borne by the community.

In dealing with fractures, continuity of treatment is of the first importance. The disabilities of the terminal stages of convalescence must be recognized in their incipient form in the first days of treatment; no improvement can be expected until, in every general hospital, the whole of the treatment of fractures, from first to last, is supervised by one and the same surgeon, who is, moreover, interested and experienced in such work. I am sure if there is the will to do, there should be no difficulty in the establishment of such a routine.

*Soft-tissue injuries.*—Soft-tissue injuries are no less incapacitating than fractures; their importance to industry and the future earning

capacity of the victims is just as great, and since they outnumber fractures in the proportion of 5 or 10 to 1, the problem they present is much greater. The term soft-tissue injuries includes injuries of muscles, lacerations, infections of the hand, burns, tendon and nerve injuries, etc.

The principles of continuity of treatment and after-care as applied to organized fracture-treatment should be equally applied to these disabling injuries until working and earning capacity has been restored.

Too often and in many hospitals, the medical officer in charge of the casualty department is the most junior of the staff. He is given the great responsibility of treating wounds, lacerations, and soft-tissue injuries, unguided and unaided by the senior members of the staff. Young and inexperienced surgeons who would hesitate to remove an appendix accept the far more difficult and critical task of treating wounds, and infections of the fingers and hand, and suturing severed nerves and tendons.

Even to-day, in many hospitals in India, casualties attend hospitals in large numbers for daily dressings, with no close supervision of progress, no attempt to graduate activity, no organization of after-care, and no semblance of rehabilitation.

It is a sad reflection on our present-day system of medical education that undue stress is laid on symptomatology, diagnosis and treatment of abstruse and comparatively rare conditions, to the neglect of soft-tissue injuries and infections, which are more common and come within the daily purview of every medical practitioner during the whole of his professional career.

I regret to say that it is a customary practice in the casualty or out-patient department of many general hospitals in India to allow all types of cases, casualties and ordinary sick, to sit on benches or forms in rows, surrounded by wailing relatives all waiting their turn to go into a treatment or dressing room, usually a cramped space, there to sit in a chair while wounds are stitched, dressed or fomented, often within sight and always within sound of others whose septic fingers are incised and in some cases fractures manipulated.

How can we remedy this? More attention should be concentrated on the teaching of these subjects to medical students, impressing the practical importance of treatment of such injuries in out-patient clinics, and on the reorganization of the accident service in industrial cities, and in hospitals attached to medical schools particularly, and larger towns generally. What this service should be is briefly described below.

*Medical rehabilitation.*—Plato wrote 'This is the greatest error in the treatment of sickness, that there are physicians for the body and physicians for the soul; and yet the two are one and indivisible'. How many of us realize to-day

and practise what Plato said two thousand years ago. In order to obtain good and early functional results, every injury should be regarded as physical and psychological, and the body and the mind should be treated at the same time.

Physical treatment must of course be completed. The patient must be told about his disability; he must be reassured; his fears and misgivings must be dispelled and must be inspired with hope and confidence. He should have freedom from fear and freedom from want. He should be 'rehabilitated'.

In recent years, considerable interest has been aroused in 'rehabilitation'. This word, unfortunately, is used by different people in different senses. The object of rehabilitation is to cure or reduce disability resulting from injury so that the injured person is enabled to return to his ordinary work in the industry or trade in which he was formerly employed or, failing that, to useful alternative work in the same industry or trade. It should not be used to denote the training of cripples for special occupations adapted to their disabilities; such training is called vocational training, which is essentially a process of compromise with disabilities that must be accepted as permanent. However, vocational training may be required in a very few cases where rehabilitation has failed.

Rehabilitation is a process which accelerates restoration of physical fitness after disease or injury, and should begin on the day of the injury and cease with the patient's return to his full previous activities. Intelligent rehabilitation depends on good analysis of functional disability, and this in turn depends on a knowledge of the anatomy of function and of the effects of trauma on soft tissues.

A review of results from well-established rehabilitation centres, will convince anyone that the key to success is restoration of muscle power, and this can only be ensured by active movements. It will be realized that a stiff joint with powerful muscles is less disabling than a mobile joint with powerless muscles. The function of a muscle is not only to move a joint but to protect it.

The first object of treatment, therefore, is to regain muscle control; the second is to increase the range of movement within the limits of muscle control. Progressive remedial exercises form a basis of treatment; they will only succeed, and recovery will only come, if they are performed day in and day out by the unremitting efforts of the patient himself.

In the process of rehabilitation, the aim should be not only to treat the disease or injury and heal the damaged part, but at the same time to maintain both the physical and mental fitness of the patient, and, when convalescence is established, to make good without delay the loss in strength and efficiency that has occurred. The treatment should be intensive and individual, and should consist of graduated and progressive

remedial exercises, occupational therapy, physiotherapy and recreational activity in the form of remedial games.

Hitherto, for the most part, doctors have taken little interest in this form of remedial therapy. They have had little opportunity of studying this form of treatment and of learning how to prescribe it particularly in this country. The majority of patients struggle on, often sympathetically supported but never actively helped by the doctors. Whatever the interest of medicine in remedial therapy, its practical aim is to help patients to the utmost.

Rehabilitation is a social issue, and the medical profession in the country should take more interest in it, and give the lead in their practices and hospitals. Hospital authorities, local bodies and lay administrators should be persuaded to recognize and realize that remedial therapy is an essential part of medical treatment. They will need guidance, now and after the war, on the accommodation, staffing and equipment required for these methods of treatment. Such guidance can be given only by doctors responsible for the care and welfare of the patients; the more experience the medical profession can obtain, and the more interest it takes in the practical details, the better will be the guidance and the more efficient the treatment.

#### *Organization of fracture, accident and rehabilitation clinics*

*Fracture service.*—The reports of the British Medical Association Fracture Committee, 1935 and the Delevinge Committee, 1937-39 have very clearly laid down certain principles which should form the basis of any organized fracture service.

These are :—

(a) All fractures (except of the head) should be segregated in a single department which would provide for both in-patients and out-patients.

(b) The service should be operated and controlled by a single team under a surgeon-in-charge.

(c) The treatment should be continued until restoration of working capacity has been effected to the fullest possible extent.

(d) A system of records of cases, which will permit the history of each case to be followed from start to finish and the final results ascertained, should be adopted.

The principles of treatment should be—

(a) Securing exact reduction of fracture.

(b) Fixation in correct position and immobilization of the broken part.

(c) Active movement from the earliest possible moment of the injured parts of the limb, to prevent wasting of muscles and stiffness of joints.

Fracture work should be entrusted only to the man who enjoys dealing with them. He must



accept personal responsibility and not be content to delegate the actual work to juniors. Under a man who continues to study the work of colleagues at home and abroad, always learning and always improving, good results will be obtained with the simplest apparatus; without him, the most highly organized clinic cannot rise above the mediocre. It is on lines such as these that we should like the fracture-clinic to develop.

It will be appreciated that the standard of work of a fracture department depends primarily upon the detailed supervision and the personal direction of the treatment of cases by the surgeon-in-charge. It is, therefore, essential that a fracture unit in any institution should remain single with regard to its habitat and executive personnel. The registrar, the house surgeon, the trained nursing staff and the physiotherapeutic assistant can become skilled only by dealing with large numbers of cases under the supervision and guidance of the surgeon-in-charge.

If a fracture-clinic is to maintain its efficiency, it should handle not less than 300 cases a year. It is realized that this may be possible only in large cities and industrial towns. Every teaching hospital should have a fully staffed and equipped fracture-clinic. A general hospital in a city may need from 5 to 10 beds for each 500 cases of fractures dealt with yearly. There should also be provision for the immediate treatment of shock (resuscitation). Similarly, general hospitals with 200 or more beds should have a fracture-clinic. The hospital should also have provision for remedial exercises. Ideally, the fracture department should have its own gymnasium for remedial exercises and its own physiotherapeutic department.

Hospitals with fewer than 100 beds, and hospitals in district places and rural areas, present a very difficult proposition. It is not possible to lay down any definite scheme for such hospitals. Local conditions, and the proximity or distance from the nearest larger hospital, and the experience and the qualifications of the staff will have to be taken into consideration in assessing their usefulness either to give only the first-aid treatment and send cases elsewhere, or to receive a visiting fracture team from the nearest larger hospital, where such exists. A delay of one or two days is permissible in a case of simple fracture, but a compound fracture is a serious surgical emergency requiring immediate operative treatment within six hours.

The crux of the problem is that either the patient must be brought to the fracture-surgeon at the nearest hospital, or the fracture-surgeon must visit the patient in the rural hospital. It would be an advantage if we could have a fracture service on a regional or divisional basis serving a group of smaller hospitals, and with its headquarters at a district place with a larger hospital.

Very briefly, the essential units of a fracture-clinic may be described as consisting of the examination room with some cubicles, the fracture theatre and plaster room, x-ray room, physiotherapy section (gymnasium and massage). These rooms should be as close as possible, particularly the first three. Such an arrangement will improve the efficiency and the speed of of the clinic as a single full unit by the surgeon-in-charge.

*Soft-tissue injuries, casualty department.*—As previously observed, soft-tissue injuries are far more common and no less incapacitating than fractures. The problem of their treatment is equally important, and, if we are to achieve good results in injuries entailing disablement, we should revise our ideas about the casualty or accident departments of general hospitals.

The casualty department in most hospitals in India needs reorganization and replanning with regard to staff, equipment, and accommodation.

The principle of organization, continuity of treatment, and unity of control as applied to fracture-clinics should be equally applied to casualty departments. The department should be in the charge of a surgeon, who should have a good general knowledge of every branch of surgery and some experience in fracture and orthopaedic work. It would be a great advantage if he is specially trained in the problems of trauma. Since in larger cities and industrial towns and teaching hospitals the department will have to provide a twenty-four hour service, the surgeon must be aided by an assistant, a registrar, house surgeon and house physician and the nursing staff. He should also have secretarial and clinical assistance.

Close liaison will be required with other departments in the hospital, e.g. physiotherapy, rehabilitation clinic, and with the general practitioner and with the industrial and insurance medical officers.

For the proper functioning of such a unit, the following accommodation will be necessary. (a) Casualty reception and examination room, where a casualty is admitted whether he arrives by ambulance, by car or on foot; cubicles, couches, and chairs should be provided in this room. (b) Dressing and treatment room. (c) Minor surgery theatre, and (d) Waiting room for relatives.

*Rehabilitation clinic.*—The object of rehabilitation is to cure or reduce the disability resulting from trauma or disease to such an extent that the patient is enabled to return to his ordinary work as early as possible. As previously observed, the psychological aspect of the trauma should not be neglected.

The commonest cause of disablement is an injury. The physical treatment must be completed, and if function is to be restored in the shortest possible time, muscular wasting and joint stiffness must be prevented; union of a fracture in a perfect position means little to a



patient until he has regained the activity of his muscles and the normal movements of his joints.

The key-note of treatment is activity in the form of progressive remedial exercises and games. This requires careful thought, planning and supervision. Each patient should be studied carefully and individually; with his co-operation, progressive and gradual remedial activity will restore function in the shortest possible time. Without this, any form of passive treatment will have very little effect.

Rehabilitation centres should be established in every large city and industrial area. In establishing rehabilitation centres, care must be taken that they do not become the modern counterpart of the massage department, which too often degenerates into a dumping ground for fractures in which the surgeon's interest has vanished. Otherwise rehabilitation centres will prove no less futile than massage departments in curing complications which should never have arisen.

The principal requirements for conducting a rehabilitation clinic are: (a) accommodation for indoor and outdoor exercises and games and (b) equipment for occupational therapy. It will require a fully trained staff, medical and ancillary, e.g. surgeon-in-charge (necessarily one experienced in fracture and orthopaedic work), house surgeons, fully trained sister, masseuses, physical training instructors, and occupational therapist. It is quite possible that at present, such a staff may not be available in sufficient numbers, even in larger and teaching hospitals.

The alternative is that we should make a beginning now at least in large industrial cities. If there are several hospitals in a city, the most suitable one from the point of view of staff and accommodation should be selected as a 'rehabilitation centre'. The best possible arrangement in view of existing circumstances would be that cases from other hospitals requiring 'rehabilitation' should be sent to this centre. There should be close liaison, understanding and frequent consultations between the staffs of the 'centre' and other hospitals.

The above may be regarded as an interim arrangement until such time as other hospitals can provide necessary staff, equipment and accommodation to institute their own clinic.

The problem of smaller hospitals in the mofussil is a difficult one. They should adopt such modified methods as may be applicable to local conditions, bearing in mind the importance of remedial therapy as an essential part of treatment of all injuries and certain diseases.

The principles and process of rehabilitation of the injured may be briefly described as follows:—

(1) During immobilization: earlier measures should be directed to the conservation of muscle function; in fact, rehabilitation should really begin with the initial treatment of the fracture.

(2) The object is to provide the patient with a period of graduated work, under constant

medical supervision, up to the full stress of the original occupation, i.e. restoration of full working capacity.

(3) A patient should be visualized as a social entity, and he should have freedom from fear and freedom from want. He would require both physical and psychological treatment. In the process of rehabilitation, the treatment should be intensive and individual and should consist of:

(a) *Remedial exercises*.—These should be gradual and progressive, and should be performed with gradually increasing resistance (the Danish system and the Swedish system).

(b) *Occupational therapy*.—Is divided into indoor and outdoor work. It will depend upon the patient's work and the nature of his injury.

(c) *Recreational activity*.—Indoor or outdoor; it should be progressive and adapted to the injury. Indoor form—arts and crafts designing, weaving, etc.). Outdoor form—games of various kinds (gymnastics, swimming, cycling, etc.).

(d) *Physiotherapy*.—Comprises massage and movements and the application of radiant heat, diathermy and faradism. These will increase the blood flow and relieve spasms and pain. They are valuable preliminaries to active exercise.

*Under-graduate and post-graduate instruction*.—I wonder how many fracture cases on an average does a medical student, even in larger teaching hospitals in India, see during his six months' surgical dressership. Many of the teaching hospitals in India do not possess an organized fracture department or clinic; this and other evidence leaves no doubt that at present the training of students in fracture work is seriously deficient.

I think it is quite possible for a student to qualify without ever having seen a fracture actually treated. It is high time that we should revise our ideas about the training of medical students in fracture work during their surgical dressership by imparting both theoretical and practical instruction.

In fact, I may suggest that if the standard of fracture surgery is to be improved, every medical student during his surgical dressership should spend at least one month in the fracture department. I feel certain that if at least one continuous month were spent in daily attending a fracture department, it would be much more valuable than the haphazard seeing of odd cases of fractures scattered over the period of his full dressership.

My above remarks relate to fractures generally, but it is also true to say that little attempt is made to impress upon students the importance of infections of the fingers and hand, or injuries of tendons and nerves. Neglect of these injuries in the earlier stages may give rise to progressive, permanent, and crippling deformities, with very adverse effects on the patient and his working and earning capacity; yet with early recognition and proper treatment, results may be obtained which in many cases may be

so dramatic that they may make impossible the recognition of the original lesion.

It is also equally true to say that the vast majority of general practitioners have little knowledge of modern principles of treatment of fractures, much less of rehabilitation as an essential part of treatment in cases of bone and soft-tissue injuries. This is mainly due to lack of training in this branch of surgery during their under-graduate years, and also to lack of practical experience on account of the limited number of residential hospital appointments available in the country, and reluctance to take advantage of what limited post-graduate clinical facilities are available.

It would be profitable if, in large teaching centres, regular and periodic post-graduate refresher courses were instituted in various branches of medicine and surgery, so as to keep the knowledge of medical practitioners refreshed and up to date.

#### Summary

In this article, methods of treatment are not questioned. It is the organization of the hospital services which has been, and in many cases still is, defective, and in which radical change is needed. Since the proved advantages of unified control are so great, in any hospital the interest of individual members of the staff should give way to the general interest of the community.

I am fully cognizant of the inherent defects as they exist at present in this country regarding equipment generally, and the availability of surgeons trained in orthopaedic work, and nursing and physiotherapeutic staff particularly; but I feel that it is high time that we should make a real start on proper lines at least in hospitals attached to medical colleges and other hospitals in large industrial centres.

It is hoped that the general principles enunciated by the British Medical Association Fracture Committee and Delevinge Committee will be accepted by hospitals, government departments and local bodies concerned, and that the object in view will be the provision of 'Fracture and Rehabilitation Service' in industrial centres and other big towns and cities, which will place within the reach of every injured person the benefit of the improved methods of treatment, with the three-fold results of mitigating suffering, reducing the period of disablement and the loss of working and earning power, and securing wherever possible complete restoration of working capacity.

Even when the 'Fracture and Rehabilitation Clinics' visualized above have been organized, set up and built up, there will still be certain cases in which restoration to full working capacity can be brought about only by the fitting of an artificial limb. The problem of provision and manufacture of artificial limbs will have to be tackled, and this will need expert technicians, expert surgical oversight and control of the

supply and fitting of an artificial limb. This is most essential if wastage is to be prevented and best figures are to be obtained.

I am aware of the magnitude of the task; we have to make a beginning, as if it were from nothing. The provision of 'Fracture and Rehabilitation Service' will call for careful planning to meet local needs and conditions. The co-operation of local authorities, hospitals, medical profession, and of employers and workers organizations will be necessary.

#### Conclusion

As man is the constant and most important factor common to all vocations and industries in peace and in war, conservation of man-power and maintenance of morale by relieving disability or incapacity of the body and soul becomes a major objective. The practical aim of medicine is to help patients to the uttermost. How this can be achieved is briefly described above in a sort of preview of things to come, somewhat ambitious no doubt, but not fanciful, and, if there is the will, easily attainable. The major considerations are money to provide the equipment, time to train the personnel, and the full recognition of remedial therapy as a branch of medicine; none of them out of reach, if public opinion and the authorities concerned consider the object worth while.

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## Medical News

### I.R.F.A. RESEARCH WORK IN 1943

#### NUTRITIVE VALUE OF DEHYDRATED VEGETABLES

DEHYDRATED vegetables are now being manufactured in large quantities in many belligerent countries and it is important that their nutritive value should be studied. A good deal of work on this subject has been carried out in the Indian Research Fund Association Nutrition Research Laboratories, Coonoor, under Dr. W. R. Aykroyd, says the report of the Scientific Advisory Board of the Indian Research Fund Association for the year 1943.

Steam-blanching cabbage was found to lose vitamin C more rapidly on storage than cabbage blanched by dipping in boiling water. Loss of vitamin C in dehydrated vegetables prepared by the so-called 'pre-cooking' method was more rapid than in vegetables prepared by other processes. The general conclusion arising out of a considerable amount of work on the vitamin C content of dehydrated vegetables is that these cannot be relied upon as antiscorbutics after a period of a few months' storage.

While carotene is somewhat more stable than vitamin C in dehydrated vegetables, very appreciable losses occur on storage. After 20 weeks' storage at 98°F. bitter melon, cauliflower, carrot, pumpkin and potato lost from 35 to 65 per cent of their original carotene content. Losses in the mineral content of dehydrated vegetables during reconstitution and cooking amounted to 60 per cent. When in the U.S.A., attending the United Nations Conference on Food and Agriculture, Dr. Aykroyd collected considerable literature on the effect of dehydration on the nutritive value of vegetables and other foods, a subject which is being intensively studied in England, Canada, the U.S.A. and Australia.

#### OTHER INVESTIGATIONS

Nutrition research work was pursued most actively, says the report, which devotes a section to the work done by a unit set up in Calcutta to investigate the best method of treatment for starvation cases.

During the year investigations continued on sprays for killing adult mosquitoes, on larvicides and on various drugs considered to be useful in the treatment of malaria.

Leprosy research included the continuation of observations on the results of different kinds of segregation and progress was also reported in work on a specific test for this disease. Advance was made in work directed towards the improvement of anti-plague vaccine. On the pharmacological side, progress was made in investigations to determine the value, if any, of indigenous drugs reported to be of use in certain diseases. For 1944-45 a comprehensive and practical programme has been outlined.

#### A GERMAN SULPHONAMIDE\*

SINCE 1941 German journals reporting experiences in wound surgery have ascribed to a substance known as marfanil, the properties of a first-class local antiseptic. Recently an opportunity occurred for a test of these claims to be made by R.A.M.C. officers, and the material they used consisted of supplies captured during the fighting in the W. African desert battles.

\* Abstracted from the *Pharmaceutical Journal*, 10th June, 1944, p. 231.

They found, and their results are reported in *The Lancet* for 13th May, p. 627, that the German claims were substantially correct, that penicillin alone gives better results than marfanil, and they recommend that a further investigation of this compound be made.

Marfanil is a simple homologue of sulphanilamide, namely 4-aminomethylbenzene-sulphonamide, that is to say, benzyl-amino-p-sulphonamide. It was discovered by Domagk, and the special feature claimed for it in the German literature (J. Klarer, *Klin. Wschr.*, 1941, 20, 1250; G. Domagk, *ibid.*, 1942, 21, 488) is that it is not antagonized by the *p*-aminobenzoic acid which is always present in pus and which inactivates all other known sulphonamide drugs. The compound is known to be particularly active against anaerobes such as the gas-gangrene organisms. Marfanil is readily produced from sulphanilamide by diazotization and treatment with copper cyanide followed by hydrogenation of the nitrile thus formed. It is a far stronger base than sulphanilamide, and gives a neutral hydrochloride which is very soluble in water and suitable for injection. The base has a melting-point of 153°C. and the hydrochloride of 265°C. The synthesis has been described by E. Miller and co-workers (*J. Amer. Chem. Soc.*, 1940, 62, 2099), but we have been able to trace no reference to its biological properties, whether *in vitro*, in laboratory animals or clinically, in the English language, until *The Lancet* article appeared.

#### U.S.A. PENICILLIN PRODUCTION\*

We understand that penicillin is now being produced by twenty American and two Canadian firms. Production is rapidly being speeded up, and in December 1943, 40 per cent of the total output for that year was achieved. Early in 1943 penicillin was sold at \$20 for 100,000 units, but in January 1944, the price had fallen to \$4.75 for 100,000 units.

The Chemical Department of the War Production Board points out that the main reason for the scarcity of penicillin is the difficulty of production; manufacture requires such equipment as refrigeration machinery, centrifuges, vacuum pumps, tanks and special packaging devices. The fermentation cycle is unusually long, and exacting conditions of sterility, temperature and atmosphere control are required to obtain a satisfactory yield. More than 20 quarts of culture fluid are required to yield one gramme of the dry powder. Work is still being done to determine the most productive strains of mould and to improve culture media, methods of extraction, purification, standardization and packaging. Ninety-five per cent of the proposed plant has now been constructed and no further major expansions are to be approved.

\* Abstracted from the *Pharmaceutical Journal*, 15th April, 1944, p. 158.

#### THE FACULTY OF TROPICAL MEDICINE AND HYGIENE, BENGAL

THE following students are declared to have passed L.T.M. Examination, Session, 1944.

##### Passed

(Arranged in alphabetical order)

1. Kamalendu Das Gupta, L.M.F., private practitioner.
2. Tara Sankar Ghosh, L.M.F., private practitioner.
3. Dharendra Chandra Gupta, L.M.F., Sub-Assistant Surgeon, Bengal-Nagpur Railway.
4. Sohan Lal Khosla, L.S.M.F., House Surgeon, Harindra Hospital, Faridkot.
5. Aleyamma Mamen, L.S.M.F., Medical Missionary, Christudas Ashram, Palghat.
6. Joydeb Mukherjee, L.M.F., private practitioner.
7. Sukumar Mukherji, L.M.F., Assistant Medical Officer, Teesta Valley Tea Co., Ltd., Rangli Rangliot, District Darjeeling.
8. Om Parkash, L.M.F., private practitioner.
9. Syed Abdul Hafeez Salfi, L.M.F., House Physician, Darbhanga Medical School, Darbhanga.
10. Amar Nath Soni, L.M.F., private practitioner.

## Public Health Section

### KALA-AZAR IN BENGAL: ITS INCIDENCE AND TRENDS

By P. C. SEN GUPTA, M.B. (Cal.)

Officer-in-charge, Kala-azar Research Department,  
School of Tropical Medicine, Calcutta

#### Introduction

KALA-AZAR is believed to have existed in Bengal for over a century now.

Earliest records of a disease that was certainly kala-azar show that there was an outbreak of fever that was known as *Jwar-vikar* in Jessore in 1824-25, and in three years this epidemic devastated the division causing it is said the death of no less than 750,000. French in his report dated 1868 mentioned the Jessore epidemic and stated that eight years later the disease appeared in Nadia and in 1857 in Hooghly and finally reached Burdwan in 1862. The disease is said to have been introduced in the Dacca district in 1862, by the crew of a country boat who came from up-country to Jagir, a market town on the Dhaleswari river, all of whom died of a low remittent fever. The disease spread over the villages and towns of the district, decimating the population, and in four years the once busy town had ceased to exist. In North Bengal the disease was apparently prevalent at Dinajpur and Rangpur in 1872. In Bihar, it was known to be prevalent about 1882. From Bengal the disease apparently spread up the Brahmaputra Valley in the wake of the British conquest of Assam and improvement of communications with Bengal, and came to be known as '*Sarkari bemari*', the first outbreak taking place in 1869 in the Garo Hills (Scott, 1942). That the disease existed elsewhere in India and abroad was realized only after the discovery of the parasite *Leishmania donovani* in 1903.

Bengal has thus been the oldest known kala-azar area in the world. But reliable statistics have not been available until the very recent years. It was in 1921 that arrangements were made by the medical and public health departments for the collection of data relating to the number of kala-azar cases treated by the various government dispensaries and hospitals but it took three years for the scheme to yield satisfactory data. Napier (1923), making what he called a rough estimate of the incidence of kala-azar, was of the opinion that the total number of cases was at least 1.5 millions. He based this figure on (what may be called a 'sample survey') the records of a kala-azar treatment centre near Calcutta. A 'sample survey' based on the findings in one area has the great disadvantage in that the incidence of a disease may vary widely in the different districts, and thus an estimate of incidence based on it may not be applicable for the whole province.

The figures published by the public health department, relating to the number of kala-azar cases treated by the various state dispensaries and hospitals in the different districts of Bengal, may be taken as fairly reliable from the year 1924, and these represent the large majority of cases occurring in Bengal. A proportion of cases is treated privately by medical practitioners, but the number of such cases is in all probability, quite small in comparison with the number of cases attending the state hospitals and dispensaries.

The figures obtained from the hospital and dispensary statistics will be quite adequate for the estimation of the relative prevalence of the disease in the different districts, but in calculating the incidence of the disease in Bengal, the figures will fall short of the actual number. The figures for Calcutta, however, do not represent the actual number of cases, because large number of patients from the districts come to Calcutta for treatment.

In this paper it is proposed to estimate the incidence of kala-azar in Bengal and in its various districts and to examine the trends of incidence.

The calculation of incidence is based upon the dispensary and hospital statistics from the years 1931 to 1940 published by the Government of Bengal, and the indications of the trends of incidence on the different districts obtained from the same figures for the years 1924 to 1942.

#### The incidence of kala-azar in Bengal and its various districts

For a disease like kala-azar, the figures relating to a single year can not be expected to yield any satisfactory idea as to its incidence. The incidence varies sometimes widely in different years in the same area. Figures covering a period of several years have considerable value. Moreover, figures are not likely to be exaggerated by the same patient appearing in several years. A patient cured of kala-azar does not often develop a second attack of the disease.

The population of the districts (and consequently of the province) has also varied from year to year.

To estimate the incidence of kala-azar in Bengal, the total number of cases during the ten-year period 1931 to 1940 has been used; the population of the districts and of the province has been taken as the mean of the populations enumerated in the censuses of 1931 and 1941. From these two, the average number of cases per 100,000 population per year (specific morbidity rate) has been calculated for each district (see table II). The figures relating to Cooch Behar and Tippera States are not available, and those relating to Chittagong Hill Tracts inadequate, so these areas have been omitted.

The map (see figure 1) reproduced below is based on the figures in table II. This may be regarded as the kala-azar map of Bengal for the period 1931 to 1940.

It will be seen that the incidence of the disease is far from uniform in the different districts of the province. It is very low in the districts of Bankura and Birbhum which abut on the laterite hilly districts of Behar and where the soil is laterite-containing. The worst affected districts appear to be Murshidabad, Malda and Rajshahi. Jessore, where the first epidemic was reported to have taken place, is

TABLE I  
Number of kala-azar cases admitted for treatment

Districts	1924	1925	1926	1927	1928	1929	1930	1931	1932	1933	1934	1935	1936	1937	1938	1939	1940	1941	1942
Burdwan	1,513	2,033	2,294	3,234	3,078	2,648	3,340	3,407	2,373	2,679	4,187	2,299	1,832	1,428	899	2,361	1,902	797	813
Birbhum	79	44	34	47	41	44	64	54	63	74	91	98	67	68	95	97	70	88	86
Bankura	37	60	165	2,048	46	66	100	138	101	71	65	441	80	28	21	34	28	18	15
Midnapur	193	440	438	2,617	1,453	1,217	1,179	1,258	1,097	1,025	770	441	447	194	123	96	91	44	95
Hooghly	7,445	5,031	3,896	4,388	5,532	3,622	3,760	3,249	2,339	2,460	2,154	485	1,308	1,170	932	1,074	949	1,892	2,957
Howrah	5,675	4,327	2,558	3,632	2,738	1,808	1,207	955	765	816	947	347	139	93	79	68	106	51	58
24 Parganas	18,324	27,950	24,709	25,584	20,789	14,384	11,303	9,155	5,873	7,737	2,587	2,295	2,009	1,014	1,491	1,007	989	1,071	539
Calcutta	8,133	11,238	9,947	13,278	12,218	10,640	6,922	6,322	4,764	5,373	6,195	5,974	5,779	3,934	3,974	4,362	4,649	3,834	5,114
Nadia	8,206	7,596	5,653	8,815	8,075	7,455	6,824	6,549	5,415	5,579	4,794	3,902	4,150	3,934	3,974	3,428	3,810	3,834	5,114
Murshidabad	1,377	2,296	3,721	2,876	2,063	2,696	3,947	5,737	9,309	9,192	9,175	7,721	5,472	5,886	6,532	5,842	6,038	5,768	9,392
Jessore	5,553	8,641	6,580	17,741	7,008	5,563	4,807	5,014	5,655	9,208	5,109	5,049	4,066	4,915	7,070	4,520	4,897	4,704	5,540
Rajshahi	3,594	8,450	9,401	6,861	4,903	3,183	3,724	4,813	5,717	7,281	5,870	5,780	5,772	3,952	3,952	3,869	4,990	4,716	5,902
Khulna	10,891	15,820	18,076	19,001	12,039	11,921	11,675	9,681	11,026	15,369	11,408	10,448	6,931	6,066	4,198	4,784	5,376	6,138	3,063
Dinajpur	2,016	2,984	3,046	3,311	4,493	3,703	2,730	2,992	3,715	6,628	7,228	5,772	6,073	5,844	6,006	6,767	7,166	6,840	6,890
Rangpur	3,306	5,224	5,385	6,584	5,642	5,436	3,479	3,356	3,433	5,528	6,111	18,255	15,413	9,401	8,103	6,058	5,965	5,392	6,814
Bogra	3,971	4,897	4,808	3,080	2,341	1,167	876	1,758	1,655	1,775	2,558	6,336	5,739	1,460	1,655	1,166	967	894	888
Pabna	592	1,194	2,981	3,726	3,499	3,752	2,376	2,748	1,496	1,039	1,553	1,663	2,661	2,655	2,434	2,450	2,517	3,637	4,894
Maldia	5,596	4,890	4,304	5,119	3,340	3,494	4,173	5,326	9,075	8,764	8,140	9,060	7,084	3,844	4,393	4,320	5,771	4,847	4,592
Jalpaiguri	204	325	833	818	1,992	1,148	1,091	748	795	958	965	818	881	869	656	782	876	685	799
Darjeeling	398	278	247	308	571	450	342	356	653	951	1,423	1,308	2,215	1,648	1,258	1,050	915	987	869
Dacca	4,977	7,559	9,021	7,617	8,100	6,098	5,403	5,980	7,290	6,524	8,010	9,474	9,324	7,456	9,190	8,005	8,300	8,834	9,132
Mymensingh	8,690	16,939	9,774	7,452	6,590	5,325	4,620	3,621	3,181	4,358	3,466	3,911	6,303	7,280	6,927	9,357	12,609	13,781	15,919
Faridpur	3,718	6,911	6,296	6,418	6,063	4,318	3,053	3,205	3,258	4,638	4,255	5,549	4,999	4,381	5,434	4,339	4,366	4,664	7,241
Bakarganj	13,518	12,859	9,293	8,963	6,456	6,008	3,963	4,588	5,334	8,822	9,161	12,557	13,463	6,503	7,526	7,460	7,119	6,592	6,326
Tipperah	14,270	19,544	9,579	8,734	8,310	4,849	4,638	5,664	5,015	4,973	5,325	6,623	6,764	6,480	7,317	5,992	5,434	4,870	3,372
Noakhali	13,563	9,437	6,274	4,964	3,012	2,419	3,011	2,726	4,663	5,807	6,086	7,505	10,357	5,832	6,925	5,492	5,490	4,451	3,882
Chittagong	532	1,328	1,754	2,429	1,578	1,401	1,411	1,751	1,780	1,910	3,421	3,527	8,515	4,361	3,810	3,445	3,401	5,037	2,561



TABLE II

Districts	Mean population, 1931-41	Total kala-azar cases, 1931-40	Specific morbidity rate
Burdwan ..	1,733,215	24,799	143.05
Birbhum ..	997,935	780	7.81
Bankura ..	12,000,680	586	4.88
Midnapur ..	2,994,870	5,542	18.5
Hooghly ..	1,245,992	16,120	19.37
Howrah ..	1,294,584	4,315	33.3
24-Parganas ..	3,125,130	34,157	110.44
Calcutta ..	1,652,812	55,475	335.64
Nadia ..	1,644,739	45,535	276.85
Murshidabad ..	1,505,603	70,904	470.93
Jessore ..	1,749,690	55,558	317.53
Khulna ..	1,784,683	51,996	291.34
Rajshahi ..	1,500,384	85,834	568.74
Dinajpur ..	1,841,132	58,791	319.32
Rangpur ..	2,736,316	81,623	298.29
Bogra ..	1,173,441	25,099	213.89
Palna ..	1,575,363	21,246	134.86
Malda ..	1,143,192	65,727	574.89
Jalpaiguri ..	1,036,435	8,348	80.54
Darjeeling ..	348,001	11,777	33.84
Dacca ..	3,827,360	79,583	207.93
Mymensingh ..	5,577,010	60,113	107.78
Faridpur ..	2,625,509	44,424	169.20
Bakarganj ..	3,244,030	82,533	254.41
Tipperah ..	3,484,937	35,921	170.98
Noakhali ..	1,962,060	60,813	309.94
Chittagong ..	1,975,167	59,587	301.65
<b>TOTAL ..</b>	<b>54,482,271</b>	<b>1,146,686</b>	<b>210.4</b>

still one of the badly affected areas. The incidence in the other districts will be evident from the map and table II. From table II, it will be found that during a period of ten years (1931 to 1940), 1,146,686 individuals had kala-azar. The mean population during this period was 54,482,271. The specific morbidity rate works out to be at least 210 per 100,000 population per year.

We are forced to the conclusion that in spite of the fact that one of the best specific drugs was synthesized 22 years ago and has been in use since 1923 or thereabouts, the incidence of kala-azar is so high that it is still one of the grave problems facing the medical and public health authorities of the province. We can hardly regard the disease as having been conquered, though we possess drugs that will cure over 95 per cent of cases.

#### *The trends of incidence of kala-azar in the different districts of Bengal (1924 to 1942)*

The graphs (see figure 2) show the number of cases of kala-azar treated in the various districts from the years 1924 to 1942.

**Birbhum and Bankura.**—The incidence of kala-azar is so small in these districts and the numbers treated so insignificant that no useful purpose will be served by trying to follow its trends.

**Burdwan.**—This district, where kala-azar occurred in an epidemic form in the 'sixties' of the last century, shows 2 to 3 thousand cases annually for the greater part of the period under consideration. There were a number of bad years 1930-31, and 1934. There is a

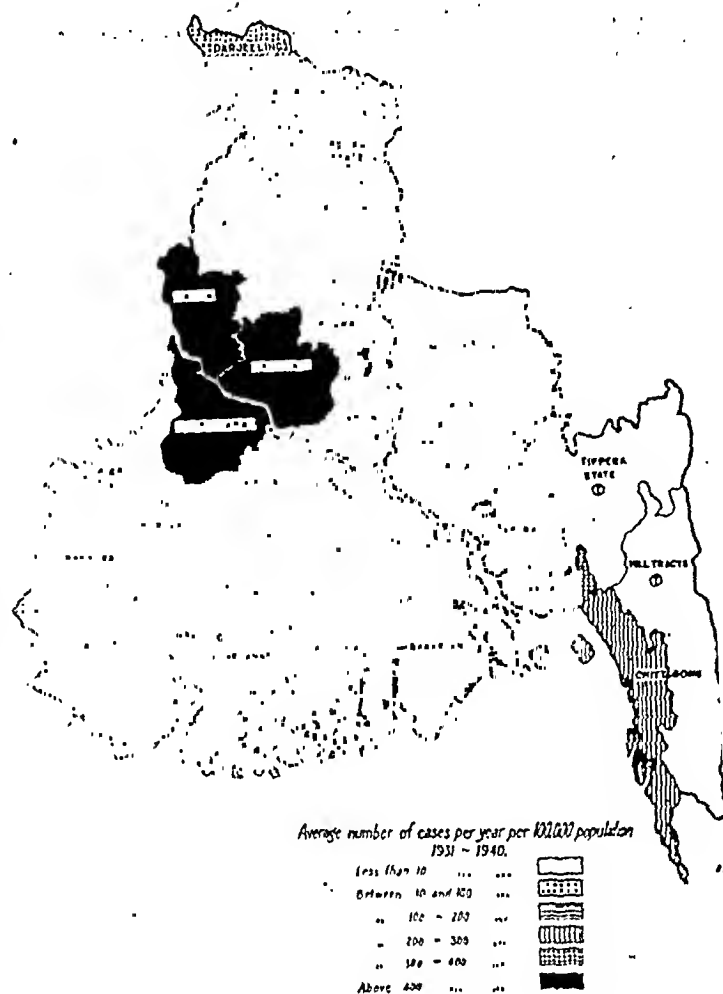


Fig. 1.—Kala-azar map of Bengal.

possibly slight tendency to decrease of the number of cases since 1935, though the number reached the two-thousand level during 1939-40.

**Hooghly.**—On the whole, the trend has been towards a decrease in the incidence.

**Howrah.**—There has been a rapid and steady decrease in the number of cases since 1924 and since 1936 the number of cases treated in this district has been very small, less than 100 cases per year. Some cases of this district are, however, treated in Calcutta.

**24-Parganas.**—This was apparently one of the heavily infected districts in the 'twenties', but after an initial rise in 1925, probably due to better diagnosis or more people coming in for treatment, the number of cases has steadily come down, and since 1934, a low endemic level has been reached.

**Midnapur.**—There was apparently an epidemic in 1927. The number of cases has slowly decreased since then, reaching the lowest level in 1940, but since 1941 the number of cases has been on the increase.

**Murshidabad.**—This has been one of the worst affected districts. During the period under consideration, there has been a progressive increase of the number of cases, the particularly bad years being 1932-34. The trend is towards an increase of incidence in this district.

**Nadia.**—There had been a slow and slight decrease in the number of cases during the period 1924-33. Since 1934 the incidence has been more or less steady, between 3 and 5 thousand cases per year.

**Jessore.**—This district, where probably the first recorded epidemic occurred, is still one of the badly affected areas.

There are usually about 5 thousand cases per year, but there was a well-marked increase in the number



in the years 1927, 1933 and 1938. The trend is thus towards a steady endemicity with rises in incidence at intervals of 5 or 6 years.

*Khulna*.—The incidence is very similar to that of Jessore district, and the trend is towards a steady

endemicity with an occasional rise in incidence, the peaks of increase during the period being in 1927 and 1942, or perhaps 1943.

*Faridpur*.—In this district, the number of cases was almost halved during the period 1925-30, but since 1933

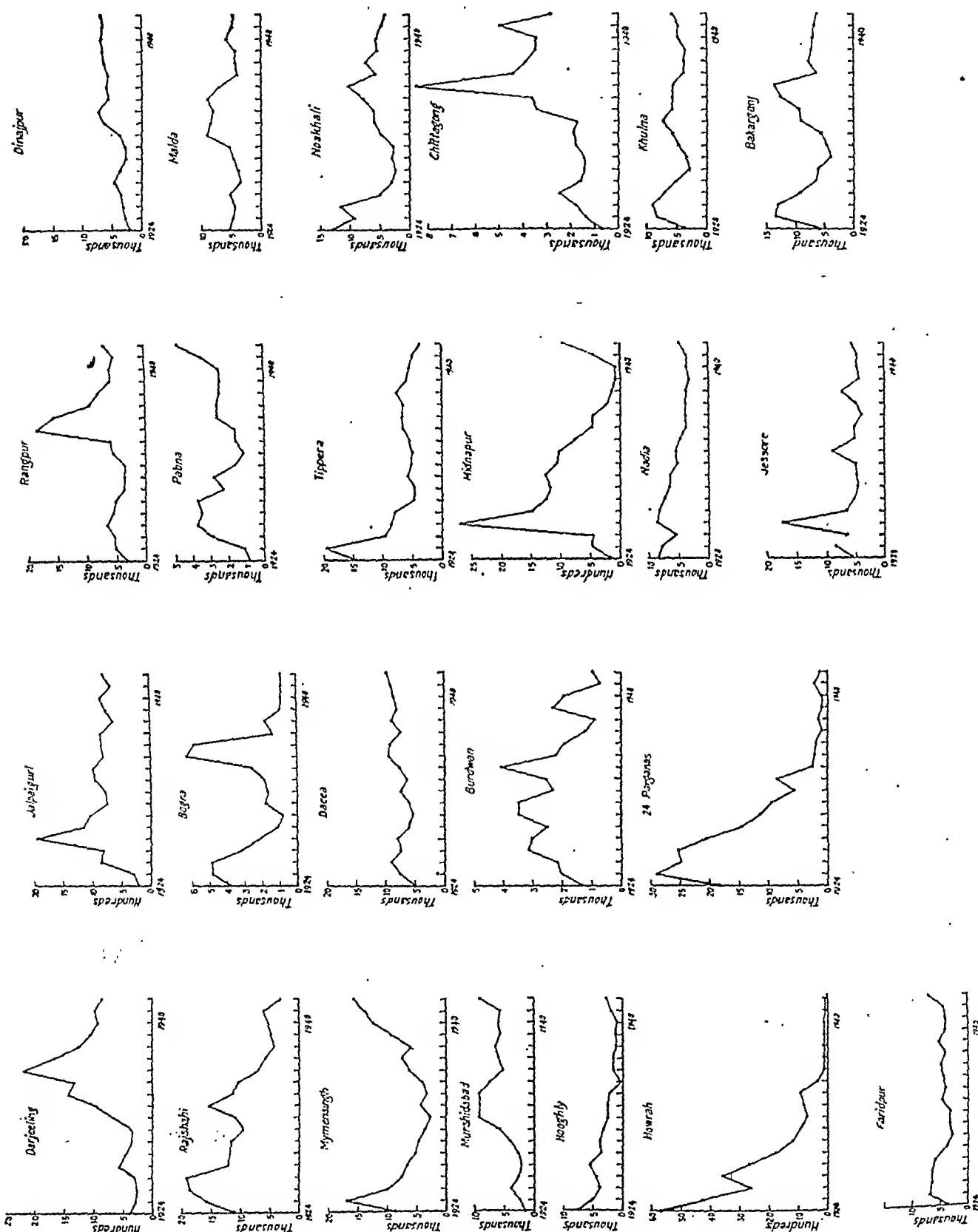


Fig. 2.—Showing the trends of incidence of kala-azar in the different districts of Bengal (1924-42).

the number has been steadily going up. The trend has been towards a slow but steady increase of incidence during the last 10 years.

**Bakarganj.**—There is no tendency to decrease of incidence in this district. There was a marked increase of incidence in 1926-27 and again in 1935-36 almost a decennial recurrence of epidemics in an endemic area.

**Darjeeling.**—Though this district shows only a low endemicity of kala-azar, the trend is towards an increase of incidence since 1932. The peak was reached in 1936, and though the numbers have been coming down gradually in the succeeding years, the level is considerably above that of 1930-31.

**Jalpaiguri.**—The incidence in 1924-25 was rather low when compared with the rest of the period. This might have been due either to an actual low incidence or to a defective mechanism of collection of data or to the sick people not coming for treatment. However, there was a marked rise of the number of cases in the subsequent years, the peak being reached in 1928. The number of cases came down in the next 2 years reaching the level of about 600 to 1,000 cases a year. The incidence during 1931-40 was 80.54 per 100,000 and this fairly represents the degree of incidence at present.

**Dinajpur.**—This is one of the badly affected districts. There has been a steady rise in the number of cases during almost the whole period, and the trend is thus towards an increase of incidence.

**Rangpur.**—There used to be 4 to 6 thousand kala-azar cases per year up till 1934. There was an epidemic in 1935 that gradually subsided during the next 3 years and the previous level was reached in 1939. The number is still over 5 thousand cases per year.

**Pabna.**—There was a progressive increase in the number of cases from 1924; the maximum was reached during 1927-29. Then the number of cases came down, reaching almost the original level in 1933, but since then the number is increasing steadily, and a level higher than that of 1927-29 was reached in 1942.

**Bogra.**—There was a marked increase in incidence in 1925-26 and again in 1935-36. The number of cases during the periods between the epidemics is in the neighbourhood of 1,000 cases per year. This district also shows the phenomenon of occurrence of epidemics at intervals of ten years in an endemic area.

**Rajshahi.**—This has been one of the three worst affected areas in the 1931-40 period. Though there were two peaks of incidence in 1926-27 and 1932, the general tendency has been towards a decrease of incidence.

**Malda.**—There was an increase of incidence from 1932-36. The tendency is for a steady level of endemicity, and it is likely that there will be periods of increase of incidence as in Jessore or Bakarganj districts.

**Mymensingh.**—There was a peak of incidence in 1925, since then the numbers gradually decreased till it reached the lowest level in 1932. The number of cases has been increasing since 1933, and the trend is towards a progressive increase of incidence.

**Dacca.**—In this district, the disease has been endemic probably since the 'sixties' of the last century. During the period under consideration, there have been between 5 and 10 thousand cases per year. The trend is towards a slight but progressive increase of incidence.

**Tippera.**—There was an epidemic(?) in 1925. The number of cases came down in the next 4 years. Since 1929 the incidence has been more or less steady, the number varying between 5 and 7.5 thousand.

**Noakhali.**—There were two periods of increase of incidence during 1924-42, the peaks being reached in 1924-26 and 1936. There were usually 2 to 3 thousand cases annually during the 'good' years. The trend is towards the occurrence of epidemics approximately every 10 years.

**Chittagong.**—There was apparently an epidemic, the peak of which was reached in 1936. The number of cases came down in the next 3 years, but there was again a rise in 1941. On the whole the trend is towards an increase.

### Summary

The incidence of kala-azar varies markedly in the different districts of Bengal. The districts of Birbhum and Bankura which are adjacent to the laterite hills of Behar and Orissa are almost free from kala-azar, the decennial incidence being less than 1 per mille. The specific morbidity rate varies from 18.5 to 568.7 in the different districts. It is thus not proper to label the whole of Bengal as a uniformly hyper-endemic area.

Considered as a whole, the average incidence of kala-azar in Bengal is 210 per 100,000 population per year.

### The trends of incidence

**Central, west and south Bengal.**—In the districts 24-Parganas, Howrah, Hooghly and Midnapur, the general trend has been towards a progressive decrease of incidence, except for the fact that since 1940 the number of cases has been increasing in Midnapur. In Burdwan, however, it is probably more correct to regard the degree of endemicity as more or less constant. The districts Nadia, Khulna, Jessore and Bakarganj show a chronic endemicity with a tendency to an increase of incidence every 8 to 10 years in some of them. Murshidabad and Faridpur show a general tendency to an increase of incidence, the former definitely and the latter slightly.

**North Bengal.**—The trend is towards an increase of incidence in Darjeeling, Dinajpur and Pabna districts. Jalpaiguri, Rangpur, Bogra and Malda districts show chronic endemicity with occasional occurrence of epidemics. In Rajshahi district, in spite of the fact that the incidence has been very high, the tendency is to decrease.

**East Bengal.**—The incidence of the disease is on the increase in Chittagong and Dacca districts. In Mymensingh district, the disease has been on the increase since 1940. Tippera and Noakhali districts show chronic endemicity with occasionally an increase of incidence.

### The present position and future

It will be obvious that though almost the best possible specifics have been in use for over 20 years, the incidence in Bengal is so high that kala-azar should still be regarded as a grave public health problem. Though in a few districts there is evidence that the incidence is decreasing, there are many more districts where kala-azar is at a steady level of endemicity, showing sudden increases at variable intervals, and in other districts particularly in north and east Bengal there is evidence of a steady increase of incidence.

Also, in view of the fact that pestilence follows in the wake of famine, it is quite possible that there will be an increase of incidence of kala-azar during the few years following the famine of 1943.

### Acknowledgment

The writer is thankful to the Director of Public Health, Bengal, for the figures relating to the number of cases of kala-azar admitted for treatment in the various state dispensaries and hospitals in Bengal during 1941 and 1942.

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## A National Health Service Government Proposals. (The White Paper Summarized)

(From Supplement to the *British Medical Journal*, *i*, 26th February, 1944, p. 31)

THE long-promised White Paper on 'A National Health Service' was issued by the Ministry of Health and the Department of Health for Scotland on 17th February. It is a document of 85 pages. After describing the present situation it proceeds to outline a comprehensive service for all citizens, and the central and local administrative structure of such a service. Hospital and consultant services, general practitioner service, and clinic and other services under the new arrangements are considered. There is a chapter on the service in Scotland, where the administrative structure is somewhat different from what it is in England and Wales. Of five appendices one reports the events leading up to the White Paper, drawing attention to the B.M.A.'s 'General Medical Service for the Nation' and the Interim Report of the Medical Planning Commission, which is frequently quoted in the body of the Paper. Another appendix is a financial statement, from which it appears that the total annual cost of the scheme in England and Wales is expected to be £132,000,000, and in Scotland £15,800,000, about two-thirds of which will be met from public funds and the remaining cost will fall on the ratepayers.

### THE OBJECTIVE

The object of the proposals is to ensure that every man, woman and child in the future can rely on getting all the advice and treatment and care which they may need in matters of personal health; that what they get shall be the best medical and other facilities available, and that their getting these shall not depend on whether they can pay for them or any other factor irrelevant to the real need—namely, the reduction of ill-health and promotion of good health among all citizens.

'The case for it [a comprehensive service] stands on its own merits, irrespective of the war or of other proposals for post-war reorganization, although it must form an essential part of any wider proposals for social insurance which may be put into operation.'

It is added that the proposals made in the Paper represent what the Government believe to be the best means of bringing the service into effective operation. The Government want them to be freely examined and discussed. They will welcome constructive criticism of them, in the hope that the legislative proposals which they will be submitting to Parliament may follow quickly and may be largely agreed.

### THE REASON FOR CHANGE

The main reason for change is that the Government believe that, at this stage of social development, the care of personal health should be put on a new footing and made available to everybody as a publicly sponsored service. It is still not true to say that everyone can get all the kinds of medical and hospital service which he or she may require. 'Whether people

can do so still depends too much upon circumstance, upon where they happen to live or work, to what group of age or vocation they happen to belong, or what happens to be the matter with them. Nor is the care of health yet wholly divorced from ability to pay for it'. The restricted nature of the National Health Insurance service is pointed out, also the uneven distribution of hospital services. Finally, personal health still tends to be regarded as something to be treated when at fault, or perhaps to be preserved from getting at fault, but seldom as something to be positively improved and promoted. Some of the principal of these deficiencies a comprehensive health service should, in the view of the Government, seek to make good.

There is a certain danger in making personal health the subject of a national service at all—the danger, namely, of over-organization. Yet if medical services are to be better marshalled for the full and equal service of the public, organization, with public responsibility behind it, there must be. Organization is the means, never for one moment the end. 'Nor should there be any compulsion into the service, either for the patient or for the doctor. The basis must be that the new service will be there for everyone who wants it . . . but if anyone prefers not to use it, or likes to make private arrangements outside the service, he must be at liberty to do so. Similarly, if any medical practitioner prefers not to take part in the new service and to rely wholly on private work outside it, he also must be at liberty to do so'.

### 'COMPREHENSIVENESS'

The proposed service must be comprehensive in two senses—first, that it is available to all people, and, second, that it covers all necessary forms of health care. The service designed must cover the whole field of medical advice and attention at home, in the consulting room, in the hospital or sanatorium, from the personal or family doctor to the specialists and consultants of all kinds, and it must include ancillary services of nursing, midwifery, and the other things which ought to go with medical care. It must secure, first, that everyone can be sure of a general medical adviser to consult as and when need arises, and then that everyone can get access, beyond the general medical adviser, to more specialized branches of medicine or surgery.

In two respects the new service will be less complete than was wished. There will not be enough dentists in the country for some years to come to provide a full dental service for the whole population, and there may be similar, though less acute, difficulties in getting a full service in ophthalmology. Mental health services are to be included, although, failing a full restatement of the law of lunacy and mental deficiency, their inclusion presents some difficulty.

It is added that a 'comprehensive' service does not mean that there should be no Government or private activity involving the use of the medical expert or having any bearing upon health. Two examples are given. One is factory medical inspection and the employment of works doctors. The enlistment of medical help here is part of the complex machinery of industrial organization and welfare and belongs to that sphere more than to the sphere of the personal doctor and the care of personal health. The other is the school medical service, to which similar considerations apply.

### THE ADMINISTRATIVE STRUCTURE

The new responsibility for providing the comprehensive service will be placed upon an organization in which both central and local authority take part, central responsibility lying with the Minister, and local responsibility with the major local government authorities (county and county borough councils) operating, for some purposes, severally over their existing areas, and for other purposes jointly over larger areas formed by combination. Both at the centre and locally special new consultative bodies are proposed for

ensuring professional guidance and the enlistment of the expert view. At the centre, in addition, a new and mainly professional body is to be created to perform important executive functions in regard to general medical practice.

#### CENTRAL ORGANIZATION

Direct responsibility to Parliament for the new service will rest on the Minister of Health and in Scotland on the Secretary of State. At the side of the Minister, but independent of him, there will be created a professional statutory body to be called the Central Health Services Council. Its function will be to express the expert view on any general technical aspect of the service. It will be entitled to advise on matters referred to it by the Minister and on any other matters within its province. Any general regulations which the Minister may make will be referred to it.

It is assumed that this Council will be primarily medical in its composition, but not wholly medical for it will be required to provide an expert view on, for example, hospital administration, nursing, pharmacy, and other subjects. It is thought that it might consist of 30 or 40 members, representing the main medical organizations, voluntary and municipal hospitals, medical teaching, and professions like dentistry and nursing. The members would be appointed by the Minister in consultation with the professional and other organizations concerned.

There will, also be set up a central Medical Board to perform executive functions in the day-to-day working of the general practitioner service. It will be composed, in the main, of members of the medical profession and will be the 'employer' body with which the general practitioner enters into contract in the new service. The distribution and welfare of practitioners and assistants will be its concern.

#### THE LOCAL AUTHORITY

The local organization is more complex. The new service has to include hospital and institutional services for the sick in general, for mental cases, for infectious diseases and tuberculosis, for maternity, and for every general and special hospital subject. The White Paper puts aside the suggestions which have been made in favour of a new kind of local authority of a vocational or technical character. The principles of democratic responsibility and of professional guidance must be applied to the local as to the central organization. The Government have no intention to supersede the present local government system; on the contrary, it proposes to take as the basis of the local administration of the new service the county and county borough councils. But the sizes of counties and county boroughs vary enormously, and there are some requirements in the new service, particularly in so far as they relate to hospitals, which counties and county boroughs cannot fulfil so long as they act separately, each for its independent area.

In many branches of hospital administration the need for larger areas has long been recognized by local authorities in their regional developments. Various alternatives for the form of authority for these larger hospital areas are examined in one of the appendices, but in the Government's view the only course possible at the present time is the creation of the larger area authorities by combining for this purpose the existing county and county borough councils in joint boards operating over areas to be settled by the Minister after consultation with local interests. In some exceptional cases, of which the County of London is the most obvious, no combination will be necessary. This does not mean that standard-sized areas can be prescribed for hospital services. Local conditions must determine size and shape.

Reasons are given why infectious diseases hospitals must in future form part of the general hospital system. 'The small isolation hospital of the past century is not only uneconomic in days of rapid transport, but cannot be expected to keep abreast of modern methods'. One result of the new outlook will be the

development, in addition to the larger isolation hospital serving the densely populated area, of accommodation for infectious diseases in blocks forming part of the general hospitals.

#### LOCAL CLINIC SERVICE

The case for centralizing all administration in one authority over the larger area does not hold to the same extent in the case of services given in local clinics or by domiciliary visiting. Nevertheless, this services should be regarded in future as the related parts of a wider whole, and should fit in with all the other branches of a comprehensive service in their planning and distribution. The new joint authority will therefore be charged to examine the general needs of the area from the point of view of the health service as a whole, including in addition to hospitals, these more local services. Normally, however, their provision and maintenance will rest with the individual councils, and the joint authority will be concerned only to watch that the general area arrangement proves to be the right one when put into actual operations.

Some forms of local clinic service, like tuberculosis dispensaries, mental clinics, and cancer diagnostic centres, are in essence out-patient activities of the hospital and consultant services, and these should usually be the responsibility of the same authority as is responsible for the hospitals and consultants over the larger area. But, generally speaking, no hard-and-fast rule can be applied.

Special considerations apply to the general practitioner branch of the new service, which is reviewed in detail later in this summary. The main aspects of the service which affect the individual practitioner, including the terms of his participation, the protection of his professional interests and his general personal relationship to the new service, will be governed by central arrangements applicable to the country as a whole. But there is no question of excluding this branch of the health service from the concern of the new joint authorities to plan for the requirements of their services. The provision and maintenance of health centres for grouped medical practice would be a function appropriate to individual county and county borough councils.

#### PROFESSIONAL GUIDANCE

Just as there is to be centrally a Health Services Council so there should be similar consultative machinery for local administration. The purpose of the Local Health Services Council will be to provide a medium for expressing the expert point of view on technical aspects of the service. Provided that all the professional interests are fairly represented, there is no reason why the pattern of these bodies should be uniform throughout the country.

The Government turn down the proposal that on the local administrative authorities themselves there should be a number of members appointed by professional organizations, with or without voting powers. The risk of impairing the principle of public responsibility, that effective decisions on policy must lie with elected representatives answerable to the people, is held to be too great.

#### HOSPITALS: AN END TO ANOMALIES

The term 'hospital services' in the White Paper includes all forms of institutional care of every kind of sickness and injury. It includes also out-patient treatment and treatment at sanatoria and rehabilitation centres. The inclusion of mental hospitals and mental deficiency institutions presents many problems, calling for some degree of special organization to meet them.

The present hospital services are detailed in an appendix to the Paper, in which the need for co-ordination and better distribution is pointed out. 'The anomalies of large waiting lists in one hospital and suitable beds empty at another, and of two hospitals in the same area running duplicated specialist centres which could be better concentrated in one more highly equipped and staffed centre for the area, are largely

the result of a situation in which hospital services are many people's business but nobody's full responsibility'.

Two main problems are presented: to bring together in suitable areas the activities of the various separate and independent hospitals, and to enable two quite different hospital systems (the voluntary hospitals and the municipal) to join forces in future in a single service.

#### THE VOLUNTARY HOSPITAL IN THE PLAN

It is acknowledged that without the collaboration of the voluntary hospitals it would be many years before the new joint authorities could build up a system adequate for the needs of the whole population. From that point of view alone, therefore, the co-operation of the voluntary hospitals is a necessity. But the matter cannot be regarded from that point of view alone.

'The voluntary hospital movement not only represents the oldest-established hospital system of the country, but it attracts the active personal interest and support of a large number of people who believe in it is a social organization and who wish to see it maintained side by side with the hospitals which are directly provided out of public funds. It is not merely that the best of the voluntary hospitals have, in a degree so far unsurpassed, developed specialist and general hospital resources which they will be able at once to make available [but], most of the rest of the voluntary hospitals have experience and an existing organization which it will be obviously sensible to enlist. It is certainly not the wish of the Government to destroy or to diminish a system which is so well rooted in the good will of its supporters.'

Yet the responsibility for a comprehensive service accepted by the community may affect fundamentally the position of the voluntary hospitals. A new universal public hospital service, says the White Paper, might have the gradual effect of undermining the foundations on which the voluntary hospitals are based. If this is not to happen a way must be found of combining the general responsibility of the new joint authority for the service with the continued participation in that service of the voluntary movement as such. The whole service must be brought under one ultimate public responsibility without destroying the independence and traditions to which the voluntary hospitals attach value. The Government believe that this can be done.

#### SELF-SUFFICIENT HOSPITAL AREAS

The joint authority will assess in detail the hospital needs of its area and the resources available; then it will work out a plan of hospital arrangements, based on using, adapting, and, where necessary, supplementing existing resources. The plan must ensure, for instance, that the various special treatments are concentrated in centres competent and convenient to provide them, not dispersed haphazard in uneconomic and overlapping units. The area will be made as self-sufficient as possible. The joint authority will secure the necessary service for its area partly through its own hospitals and institutions and partly through contractual arrangements made with the voluntary hospitals. The plan will be submitted to the Minister for approval, and the Minister will have regard to its relation to the country as a whole. No voluntary hospital will be compelled to participate. If it does agree to participate it will do so under certain conditions, which will apply also to the authority's own hospitals; for example, each hospital will agree:—

- (1) To maintain the services which it undertakes to provide under the plan;
- (2) To observe national requirements with regard to payment and conditions of its nursing and domestic staff;
- (3) To conform with any national arrangements in appointing senior medical and surgical staff;
- (4) To be open to visiting and inspection in respect of its part in the public service;

- (5) To have reasonable uniformity in accounts and audit. (This applies to voluntary hospitals; the presentation of accounts of municipal hospitals is largely subject to central direction.)

It is the aim of the Government to enable voluntary hospitals to take their important part in the service without loss of identity or autonomy. But they must still look substantially to their own financial resources, to personal benefactions, and the continuing support of those who believe in the voluntary movement. This being understood, the financial relation between the joint authority and the individual voluntary hospital must be that of an agreement to pay a specified sum in return for services rendered, and this should not be assessed as a total reimbursement of costs incurred. In addition both the municipal and the voluntary hospitals will receive a direct grant from public funds which will include the share attributable to hospital services of any sum allocated towards the cost of the comprehensive health service from the contributions of the public to any scheme of social insurance.

For the inspection of hospitals—a formidable task seeing that there will be hundreds of them under different managements taking part in a public service—a suggestion is made for the appointment of a body of persons, some on a whole-time and others on a part-time basis, and grouped in suitable panels for operating over an area.

#### CONSULTANTS: PLAN NOT YET READY

One of the duties of the joint authority will be to ensure that, through the various hospitals taking part, there will be provided an adequate consultant service available to all general practitioners working under the plan. The local service payments to hospitals will be based on the assumption of a consultant staff properly remunerated to enable the hospital to fulfil its tasks.

The Government are awaiting the report of Sir William Goodenough's Committee on Medical Schools before proposing in detail a form of consultant service. There is need, says the Paper, for more consultants and a better distribution of them. One of the aims of the service will be to encourage more doctors of the right type to enter this branch of medicine or surgery and to provide means for their training. The consultant service will still need to be organized with the medical teaching centre as its focus, but it must be spread over a wider area. The consultant taking part in the service must be associated with his particular hospital or hospitals on a much more regular basis. His function will be normally one of regular and frequent visiting of his hospitals, both for in-patient and out-patient consultation, and of visiting outlying 'general practitioner' hospitals. Remuneration may be on either a full-time or a part-time basis; there will be no need to make either form of appointment a universal rule. Some degree of control of the discretion of individual hospital authorities in making appointments to senior clinical posts will be required. The danger of 'in-breeding' under existing practice is recognized. An expert advisory panel should recommend a number of suitable candidates, from whom the hospital authority would make the final choice. One or more representatives of the appointing hospital could join the panel dealing with the sifting of candidates, the panel being based broadly on the medical teaching centres and representing both consultants and teaching organizations.

#### GENERAL PRACTITIONER ARRANGEMENTS

##### *The 'Front Line' of the Service*

The 'most difficult problem of all' is the arrangement for general medical practice in the comprehensive medical service, partly because this is the 'front line' of the service, and, partly because, notwithstanding National Health Insurance experience, the covering of the whole population creates many new problems. The doctors working a service which is free to the people and looking to public funds for their remuneration, must be in some contractual relationship with public



authority. The state must therefore take a greater part in future in regard to medical practice.

Two principles are to be observed: the present freedom of choice must not be generally diminished, and the continued practice of medicine as an individual and personal art, impatient of regimentation, must be ensured. 'Whatever the organization, the doctors taking part must remain free to direct their clinical knowledge and personal skill for the benefit of their patients in the way they feel to be best'.

The White Paper dismisses the system under which all doctors taking part in the service would be direct employees of the state or local authorities and be remunerated by salary. It is a system which could be organized, but it opens up much controversy, and many doctors would hold that it infringed the second of the two principles just stated. A universal change to a salaried system is not, in the Government's view, necessary to the efficiency of the service.

... to make unnecessarily so total and abrupt a change in the customary form of general medical practice would offend against the principle ... that the new service should be achieved not by tearing up all established arrangements and starting afresh, but by evolving and adapting the present to suit the future. They [the Government] are averse from imposing a total salaried service merely for the sake of administrative tidiness.

As for extending the 'panel' system to the whole population there are two main objections: (1) there is at present no effective means of ensuring a proper distribution of doctors, and (2) the future tendency is likely to be away from the idea of the all-sufficient doctor working alone and towards a bigger element of grouped practice and team work. The Interim Report of the Medical Planning Commission is quoted extensively on this point. The Government fully agree that grouped practices, to which numerous privately arranged partnerships are already pointing the way, must have a high place in the planning of the new service. Yet grouped practices cannot represent its entire shape. There has not yet been enough experiment, and, moreover the system could not be adopted everywhere simultaneously.

The Government intend, therefore, that the new service shall be based on a combination of grouped practice and 'separate' practice side by side, the former being likely to be found more suitable in densely populated areas.

#### *National negotiations*

All doctors in general practice who join in this new relationship with their patients must be treated on a similar footing, and the conditions to be observed and the rights to be enjoyed by them must be nationally negotiated. It is pointed out that this has been the practice under National Health Insurance; although Insurance Committees play a part in it, that service is in fact highly centralized. The Government are convinced that, broadly, the system of making major questions matters of negotiation between the Government and representatives of the profession is still the right one.

... it would be a mistake to apply to the new general practitioner service the normal canons of local government administration.

What is proposed is as follows:—

(1) Central negotiation of major terms and conditions will remain. Insurance Committees will be abolished, and doctors will be in contractual relation with a Central Medical Board (to be described later), to which they will look for their remuneration.

(2) Other functions of Insurance Committees will also fall to the Board but to avoid over-centralization, minor functions will be discharged through a local committee, on which there will be members of the local authority.

(3) The new joint authority will provide for the linking of general practitioners with hospital and consultant and other services in the area.

(4) County and county borough councils will normally have the function of providing premises such as Health Centres which are approved in the area plan.

(5) The doctor in his contract with the Board will be required to observe the arrangements of the area plan.

#### *GROUPED GENERAL PRACTICE*

The idea of the Health Centre as advocated by the Medical Planning Commission is approved by the Government, although it may be desirable also to encourage the idea of grouped practice without special premises. They intend to design the new service so as to give scope for a full trial of this new method. The object will be to provide the doctors with first-class premises and equipment and assistance. (In the financial statement it is estimated that the running costs of the centres, excluding the remuneration of the doctors, would probably not exceed £1,000,000 a year; the Government propose a 50 per cent grant for this new service, the other 50 per cent presumably being met out of the rates.) The doctors will be freed from the necessity of providing these things at their own cost.

Limitation of the permitted number of patients, whatever that may be, will apply both in the centre and outside it. Patients may continue to see their own doctor after he has joined the centre, or they may, if they prefer, select a Health Centre as such rather than a particular doctor. It need not be assumed that a doctor at the centre will be on duty only at stated periods and that at other times his patients will be attended by other doctors. The doctor will have his consulting hours and visit his patients as at present. But the grouping of practices will make a certain fluidity possible. A patient in emergency will be sure of attention even if his own doctor is not present, and arrangements will be possible for reasonable holidays and attendance at refresher courses.

The actual provision of a Health Centre will be the responsibility of the county or county borough council, but it will be for the joint authority in the first instance, in consultation with the local medical profession, to formulate proposals for centres as part of the area plan, and to submit them to the Minister.

The terms and conditions of service will be settled centrally for all doctors taking part of the new service, whether in group practice or not, and all doctors will enter into a contract of service with the central organization. The doctor practising in a centre will not be debarred from private practice outside it for those patients who do not wish to take advantage of the new facility. There is, however, one important question with regard to the method of remuneration of a doctor when practising at a centre which does not arise in the same way when he is in 'separate' practice outside. Inside a centre the grouped doctors should not be in financial competition for patients. If individual remuneration is based on mutual competition, the matter will become unduly complicated. It is considered, therefore, that there is a strong case for basing future practice in a Health Centre on a salaried remuneration or on some similar alternative which will not involve mutual competition within the centre.

#### *'SEPARATE' GENERAL PRACTICE*

In 'separate' practice the general framework of the National Health Insurance scheme will be retained, but there will have to be some important changes. A doctor in 'separate' practice will work from his own consulting room and with his own equipment, but he will be backed by the new organized service of consultants, specialists, hospitals and clinics, which he will be expected to use in accordance with the area plan. He will receive his remuneration from public funds on a capitation system, though even in 'separate' practice there may be circumstances in which it will be possible to remunerate him on a salaried or similar basis if he so desires, as, for example, in the case of a single doctor responsible for all the work in a sparsely populated area.



There will be no interference with the right of a doctor to go on practising where he is now and to take part in the public service in the area. But an unrestricted right to any doctor to enter any new practice and claim public remuneration at his own discretion would make it impossible to fulfil the new undertaking to assure a service for all. Under a scheme whereby the whole population are to be entitled to a general practitioner service, a much heavier responsibility will be thrown on the Government to see that the needs of the whole population are met.

This implies some degree of regulation of the distribution of medical resources, at least to the extent of securing that a doctor does not in future take up practice in the public service (whether by purchasing a practice or by squatting) in a locality which is already fully or overmanned. Such control can be left in the profession's own hands as far as possible, though it must be guided by public policy. A suitable machinery will be to vest it in the Central Medical Board.

Any practitioner wishing to set up a new—or take over an existing public service practice—in a particular area will seek the consent of the Board. The Board will then have regard to the need of doctors in the public service in that area in relation to the country as a whole and to the general policy for the time being affecting the distribution of public medical practice. If it is considered that the area has sufficient or more than sufficient doctors in public practice while other areas need many doctors, consent will be refused. Otherwise it will usually be given without question.

#### REMUNERATION OF GENERAL PRACTITIONERS

The remuneration of general practitioners is the subject of an appendix. It is assumed that in future the bulk of general practitioners will look to the new service for the whole, or substantially the whole, of their professional earnings. Hence whatever methods of payment are adopted—whether by capitation fee, by salary, or in some other way—the question at issue must be seen in a new light as compared with present payments for insurance work. It becomes a question of what is, on ordinary professional standards, a reasonable and proper remuneration for the whole-time services of a general practitioner working in a public service. Whether this should be worked out in terms of gross or net earnings, whether superannuation rights are to be taken into account, what adjustments are to be made for part-time work, are matters of comparative detail. When once the main figures have been satisfactorily settled, not only remuneration by capitation fee but remuneration under the salaried or part-salaried systems could be easily determined.

While a universal salaried system is not contemplated, the Government propose that doctors taking part in the public service should be remunerated on the basis of salaries or the equivalent in any part of the service in which this form of payment is necessary to efficiency. Whether payment is on a salaried or part-salaried system or on a basis of capitation fees, two principles will be observed.

(1) The doctor must be assured of an adequate and appropriate income.

(2) The system must be flexible enough to allow for proper variations attributable to extra qualifications and extra energy and interest, as well as representing the reasonable and normal expectations of general practice at all its stages.

No figures are given for remuneration except that in the appendix dealing with the finance of the scheme it is estimated in the roughest way that the cost of the extended general practitioner service will amount to £30,000,000 a year in England and Wales for doctors and chemists together. This figure may be compared with £8,400,000 for some 17,000 general practitioners and £2,400,000 for chemists in respect of 17,800,000 insured persons under National Health Insurance in 1938. This £30,000,000, by the way, will be met wholly

from central funds. The corresponding figure for Scotland is £3,200,000.

#### PRIVATE TREATMENT REMAINS

In the new service there will be prescribed limits to the number of patients whose care any one doctor can properly undertake. It is not the wish of the Government to debar anyone who prefers not to avail himself of the public service from obtaining treatment privately, nor to prohibit a doctor in the public service from carrying on any private practice, but it will be necessary to ensure that the interests of the patients in the public service do not suffer thereby. A doctor with an unusually large amount of private work, or with appointments in other branches of the public service, will be expected to work to a lower permitted limit than one who is entirely free from outside activity and is able to give his whole time to general practitioner work in the new service.

There is a strong case, especially when medical practice is remunerated from public funds, for requiring all young doctors entering practice to serve an 'apprenticeship' as assistants to more experienced practitioners. There will be many opportunities to employ such assistants in health centres where terms and conditions can be regulated. In 'separate' practices the Central Medical Board must be empowered to satisfy itself as to the proposed arrangements for the employment of an assistant.

#### COMPENSATION

It is recognized that these new proposals will, in certain cases, destroy the value of existing practices. In such cases compensation will be paid. A just claim would arise in the case of an outgoing doctor in an 'over-doctored' area, when the Board had refused consent to the sale of the practice. Another legitimate case would be that of a doctor who gave up his separate public practice to work in a Health Centre. It would be incompatible with the conception of a Health Centre that individual practices within the centre should be bought and sold, so that a doctor entering a centre will exchange a practice having a realizable value for one which he will be debarred from selling. On the other hand, a doctor entering a centre will acquire superannuation rights and other facilities of considerable value. It is a case for striking a fair balance between gain and loss and compensating him accordingly. This whole question will be discussed with the profession, together with the difficult question of instituting superannuation for doctors in 'separate' practices.

The Government also intend to discuss the question of total abolition of sale and purchase of publicly remunerated practices. It is recognized that abolition would involve great practical difficulty, and it is not essential to the working of the new service now proposed. The creation of Health Centres in itself will do much to limit the scope of the present system and afford a wide opportunity to young doctors to enter the profession without financial burdens.

#### THE DOCTOR'S CONTRACT

The Central Medical Board to which reference has already been made, will be a special executive body created at the centre from the profession and will undertake some of the administrative work of the service requiring a specially intimate link with the profession. The Board will have to be subject to the general direction of the Minister, but it will be the organization with which the doctor will deal as the 'employer' element in the service. Whether he is in grouped or 'separate' practice he will be in contract with it (though in Health Centre practice the local authority will be joined in the contract).

The details of the contract will be for discussion with the representatives of the profession, but it will need to provide:—

(1) For the doctor to give all normal professional advice and service within his competence;

(2) For him to comply with the approved area plan for obtaining consultant and specialist and hospital services;

(3) For the general kind of disciplinary machinery already familiar in National Health Insurance;

(4) For the observance of reasonable conditions, centrally determined with the profession, respecting certification and other matters which must arise in any publicly organized service.

The existing doctor will enter into the contract in respect of his existing practice; the new doctor, or the doctor entering a new practice, will first obtain the Board's consent, and then enter into the necessary contract. Termination of the contract will ordinarily be either by the doctor, at any time after due notice, or by the Board under conditions substantially similar to those now obtaining under National Health Insurance, with such extra provisions as may be necessary in the case of Health Centre practice.

The Board will also watch over the distribution of public medical practice generally. In 'separate' practices its consent will be required before a vacant public practice is refilled or a new public practice established. In Health Centres it will be the agency through which any additional doctors required in future will be introduced into any particular centre, after suitable consultation with the doctors already working there, through the local committees to which the more minor functions of the present Insurance Committees (to be abolished) have been delegated. It will be the agency through which young doctors obtain appointments as assistants at Health Centres, and by which the terms and conditions of assistants in separate practices will be protected.

Another function of the Board will be to approach medical schools and hospitals with a view to the arrangement of post-graduate and refresher courses, and yet another to act as a general centre of advice and help in the movement of doctors within the public service and in the various personal problems and requests for information which will arise. The Board will be mainly professional, but with a lay element and a few of its members will be full-time and the rest part-time. Its membership and organization will have to be finally settled by the Minister.

#### RECAPITULATION

The proposals with regard to general practice are so important that we recapitulate them shortly:—

(1) The Minister, with the new Central Medical Board, will undertake the main arrangements for a general practitioner service for the country, through which anyone who wishes to do so can associate himself with a 'family doctor' of his choice and obtain the advice and treatment of that doctor at home, or at his present consulting room, or at a Health Centre.

(2) These central and national arrangements will cover terms of service remuneration of doctors from public funds, and other aspects, and the doctor will be in contract with the Central Medical Board.

(3) The joint authority in each area will make an assessment of the needs of the area in general medical practice, keep the needs under review, and bring to the notice of the Minister and the Central Medical Board anything which seems to need their attention.

(4) The county and county borough councils (constituents of the joint authority) will be responsible for equipping and maintaining the Health Centres.

(5) Future development will include both methods of grouped and of 'separate' practice, each being developed as experience proves best in each area.

(6) Existing practitioners will be able to participate in the new service in their present areas of practice, and when they do so from their own consulting rooms they will be normally remunerated on a capitation basis, while in group practice in Health Centres remuneration will be by salary or similar alternative.

(7) Practice in the public service will not debar a doctor from private practice for such patients as request it.

(8) Limits will be fixed to the number of persons whose care a particular doctor can undertake, taking into account the extent of any private practice and other calls on his time. Higher limits will be allowed where assistants are engaged. Newly qualified doctors will normally be required to serve as assistants, and the Board will have power to require them to give full time to the public service in their early years if necessary.

(9) New practitioners wishing to participate in the service and existing practitioners wishing to do so in new areas or new practices will be required to obtain the consent of the professional Central Medical Board.

(10) Compensation for loss of selling value of practices to be payable when a doctor transfers to a Health Centre or when a public practice falling vacant is not allowed to be refilled by the Central Medical Board.

(11) Superannuation to be arranged for doctors practising at Health Centres and if practicable, for doctors participating in the service in other forms of practice.

(12) The sale and purchase of public medical practices to be discussed more fully with the profession.

The White Paper ends its section on the general practitioner service by calling for a new attitude in patient and doctor. The doctor must try to become the general adviser in all matters concerned with health no less than with disease. This means a changed outlook in much of present medical practice, but such a change cannot be effected overnight. There are signs that medical schools are beginning to realize its importance, and that a new trend will appear in undergraduate medical education. 'It will take time to develop; but it is worth stating clearly at the outset that unless this kind of medical care is ultimately provided for every person and every family, the medical profession will not be giving the public the full service which it needs and which only the medical profession can give.'

#### CLINIC AND OTHER SERVICES

A comprehensive service must include arrangements for home nursing and midwifery and health visiting and similar services. Under the new arrangements these local services will not be provided as separate entities but rather as parts of the one new general duty to secure a whole provision for health. It will be the duty of the joint authority to ensure that all these different activities are properly related to each other, to the personal or family doctor service, and to the hospitals and consultants. It will then be the duty either of the joint authority or of the separate county and county borough authorities as the case may be to provide and maintain the services on the lines of the settled area plan. There will be room for experiment and innovation. It is reasonable to look forward to the time when the general medical practitioner will be connected more closely with the services which are performed at special clinics. This kind of development will find special opportunity where grouped general practice in Health Centres is tried. There will be no closing down or abandonment of existing facilities but rather their increase and fortification.

The arrangement of lying-in accommodation in hospital or maternity home and all the institutional provision for maternity will become simply one part of the reorganized hospital and consultant services. But the ordinary functions of maternity and child-welfare clinics will not be transferred to the new joint authority but will lie wherever the related functions of child education are made by Parliament to lie under the new Education Bill. They will, however, be as much a subject as any other part of the health service for the general plan for the area. In the school medical service also the proposal will need to be related to those in the current Education Bill. The education authorities will retain as part of their educational machinery the inspection of children in the school group. But when the new health service is able to take over its comprehensive care of health the child will look for its treatment to the organization which that service provides, and

the education authority, as such, will give up responsibility for medical treatment.

Local tuberculosis centres will in future be regarded as out-patient centres of the hospital and consultant service. All isolation hospital responsibilities will similarly pass to the new joint authority as part of the general hospital problem of its area. The same is true of mental clinics. The venereal diseases service present difficulties; there are factors which point to associating it directly with the reorganized hospital service. It is a borderline case and may be left settlement in each area according to the plan.

New services which are likely to develop include a full home nursing service. Finally, with regard to the part of medical officers of health and others, it is considered that there will be an even more important part in the future for social medicine and the medical organization of public health. The new service will make great calls upon all medical men and women already engaged in the work of local health authorities.

#### THE DIFFERENCE IN SCOTLAND

The above general statement applies to Great Britain as a whole, but the new service cannot be organized on entirely similar lines in Scotland owing to difference in geography and local government structure as compared with England and Wales. In Scotland the central responsibility will rest with the Secretary of State, and, as in England and Wales, a Central Health Services Council and a Central Medical Board will be set up. Joint Hospital Boards will be formed by combinations of neighbouring local authorities to ensure an adequate hospital and consultant service and will take over all responsibility for the hospital services of the constituent authorities and also arrange with voluntary hospitals. Regional Hospitals Advisory Councils will be set up for each of the five big regions of Scotland, on which there will be equal representation of the Joint Hospital Boards and of voluntary hospitals, also of the Local Medical Services Committees which are to be set up, and of medical and medical education interests, with an independent chairman appointed by the Secretary of State. These councils will be advisory to the Secretary of State on the co-ordination of the hospital and consultant services in each region.

The Local Medical Services Committees referred to will be set up over the same areas as the Joint Hospital Boards, with representation of all local health authorities and of local medical and ancillary professions. Their function will be to advise the Secretary of State on local administration of the general practitioner service. In England and Wales the responsibility for the equipment and maintenance of Health Centres will rest normally with the county and county borough councils, but in Scotland the smaller size of the problem suggests that the centres can be provided by the Department of Health itself, at least in their initial and experimental years. But the Secretary of State will have power to delegate any of his functions with regard to the provision of Health Centres to a local authority should he think this desirable.

#### FOOTING THE BILL

The individual members of the public will be able to obtain this comprehensive health service entirely without charge, except for the cost of certain appliances. The cost will fall mainly upon central and local public funds. It will be met partly by the ordinary process of central and local taxation and partly by an insurance contribution under whatever social insurance scheme may be in operation. The Beveridge report proposed that a sum of £40,000,000 per annum should be available for the new health services. Of this £35,700,000 would be the share appropriate to England and Wales, and on the basis of a total cost of the new service of £132,000,000, as already stated, the proportions would fall as follows:—

Social Insurance Scheme	..	£35,700,000
Taxpayer	..	£48,300,000
Ratepayer	..	£48,000,000

A corresponding table for the incomplete services in 1938-39 would be approximately:

#### Contributions under N.H.I.

Acts	..	£11,200,000
Taxpayer	..	£3,000,000
Ratepayer	..	£40,300,000
		£54,500,000

Hospitals will receive from central funds payments which will include their share of the money representing the social insurance contributions of the public so far as this is attributable to hospital services. The voluntary hospitals will receive in addition fixed service payments from the new joint authority in respect of all services which they render to the scheme. For the rest they will meet the costs of their participation in the service out of their normal resources, including charitable subscriptions and donations, on which their voluntary status depends.

## Current Topics

### Indian Journal of Medical Research

Vol. 31, October 1943, pp. 125-243

- \* IMMUNOLOGICAL Skin Tests in Leprosy, Part IV, The Isolation of Three Different Protein Fractions from *Mycobacterium lepræ*, by Dharmendra, p. 125.
- \* Immunological Skin Tests in Leprosy, Part V, A Bacillary Antigen Standardized by Weight, by Dharmendra, p. 129.
- \* Bactericidal Action *in vitro* of Sulphanilamide and Sulphapyridine on *Mycobacterium lepræ muris*, by Dharmendra and R. Bose, p. 133.
- \* Studies on the Glycolytic Breakdown of Glucose in Veal Infusion, by S. N. Sen, p. 137.
- \* The Effect of Storage on the Carotene Content of Dehydrated Vegetables, by N. S. Sekhon, p. 141.
- \* Combined Estimation of Thiamin and Nicotinic Acid in Foodstuffs by Chemical Methods, by Kamala Bhagvat, p. 145.
- \* The Effect of Vitamin C on Gingival and Periodontal Disease in Indian Children, by C. D. Marshall Day and K. L. Shourie, p. 153.
- \* The Effect of 'Exercise' on the Pyruvic Acid Content of Normal and Vitamin B<sub>1</sub>-Deficient Rice-Moth Larvæ (*Corcyra cephalonica* St.), by P. S. Sarma, p. 161.
- \* Riboflavin and Pyridoxin (Vitamin B<sub>6</sub>) as Growth-Promoting Factors for Rice-Moth Larvæ (*Corcyra cephalonica* St.), by P. S. Sarma, p. 165.
- \* Accumulation of Pyruvic Acid in Rice-Moth Larvæ (*Corcyra cephalonica* St.) Fed on a Vitamin B<sub>1</sub>-Deficient Diet, by Kamala Bhagvat and P. S. Sarma, p. 173.
- \* The Role of Calcium and Vitamins in Tuberculosis: Studies on Serum Calcium in Normal and Tuberculous Subjects, by B. B. Rai and N. D. Kehar, p. 183.
- Distribution of Blood Groups among different Communities in the Government Mental Hospital, Madras, by A. R. Reddi, p. 189.
- Distribution of Blood Groups among some Donors to the Madras Blood Bank: with a Discussion on the Relationship between Neuropathic Conditions and Blood Groups, by A. R. Reddi, p. 193.
- \* On Isohaemolysis: Reports on Two Isolysins and Associated Considerations, by S. D. S. Greval, J. N. Bhattacharji, and A. B. Roy Chowdhury, p. 197.
- \* Determination of Blood Groups from Stains, by S. D. S. Greval, J. N. Bhattacharji and B. C. Das, p. 203.
- \* Standard for Papain and Its Preparations, by N. K. Iyengar, p. 211.

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In 1911, the late Professor Thompson, of Dublin, established that Bovril had the power of ministering to nutrition by the assistance it gave to the assimilation of other foods. Recently a remarkable series of experiments has been conducted at an English University. A group of medical students volunteered to undergo the unpleasant experience of allowing the passage of an œsophageal tube into the stomach so that accurate studies might be made of the effect of certain beef preparations. One of the substances investigated was Bovril.

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- \* Comparative Pharmacology of the Total Alkaloids of *Rauwolfia serpentina* Benth. obtained from Bengal, Bihar and Dehra Dun, by J. C. Gupta and B. S. Kahali, p. 215.
  - Estimation of Chlorocresol, by N. Ray and U. P. Basu, p. 221.
  - \* Cholesterol and Haemolysis, by A. C. Roy and H. K. Biswas, p. 225.
  - \* Investigations of Ground-Water Pollution, Part I, Determination of the Direction and the Velocity of Flow of Ground Water, by B. R. Dyer and T. R. Bhaskaran, p. 231.
- (Of papers marked \* the author's summary is given here.)

#### IMMUNOLOGICAL SKIN TESTS IN LEPROSY, PART IV

1. Three protein fractions have been isolated from the leprosy bacillus. These fractions are the nucleo-protein, the acid-soluble protein, and the alcohol-soluble protein. The nucleo-protein fraction has been isolated by two different methods: extraction with alkali and with a phosphate buffer at pH 6.5.
2. All the protein fractions produce allergic skin reactions of the 'tuberculin' type in cases of leprosy of the neural type.
3. Comparative tests in cases of leprosy with similar fractions of the rat-leprosy bacillus indicated that while both the acid and the alcohol-soluble proteins of the two organisms might be similar the nucleo-proteins from them differed antigenically.
4. The isolation of three different antigenically active protein fractions of *Myco. lepræ* together with the fact that one of these fractions was found to be different from a similar fraction of an allied acid-fast organism, had aroused hope that this particular fraction (the nucleo-protein) might be specific for *Myco. lepræ*.
5. The tests with the different fractions in non-contacts, however, did not show that any of the fractions was specific. This lack of specificity of the nucleo-protein fraction might have been caused by some changes taking place in it during extraction. This view is supported by the fact that the incidence of positive results in non-contacts with phosphate-buffer-extracted-nucleo-protein is markedly lower than with the alkaline-extracted nucleo-protein.
6. With improvements in the methods of isolating the nucleo-protein, the incidence of positive results in non-contacts has been markedly decreased. A specific antigen giving uniformly negative results in non-contacts has not, however, yet been isolated. The work so far gives an indication of the presence of a specific antigen in *Myco. lepræ* and encourages further attempts to isolate it in a more natural form.

#### IMMUNOLOGICAL SKIN TESTS IN LEPROSY, PART V

1. A method of preparing standard *lepromin* from dried and partly de-fatted leprosy bacilli is described. The bacilli are obtained by extracting the nodules with chloroform, storing the chloroform extract for 4 days in a refrigerator and then evaporating it, suspending the residue in ether and centrifugalizing the ethereal suspension in a refrigerator. The standardization is done by weight of the bacterial powder, 1 mg. of the powder being suspended in 10 c.c. of 0.5 per cent carbol-saline, and 0.1 c.c. of this suspension being used for the test.
2. This preparation, like the ordinary *lepromin* prepared directly from the leprosy tissue, produces both early and late reactions in the cases of the neural type of leprosy and no reactions, early or late, in cases of the lepromatous type. However, with this preparation the early reactions are stronger and the late reactions considerably weaker than the corresponding reactions produced by ordinary *lepromin*. This is considered to be an advantage.
3. The other advantages of this preparation over the ordinary *lepromin* are: the use of a more refined material, more accurate standardization and the better keeping properties of the powder (the *lepromin* suspension is apt to deteriorate on keeping).
4. It is considered that this standard *lepromin* prepared from partly de-fatted bacilli retains most of

the advantages of the protein antigens isolated from the bacilli; the extra labour and special technique involved in isolating the protein are eliminated.

5. A comparison is made of the bacterial powder obtained by the chloroform method with the powder obtained by centrifugalizing a suspension in distilled water of leprosy tissue at different densities (Fernandez method). With the chloroform method the yield of bacilli is about three times as great; and, weight for weight, the chloroform-treated bacterial powder is more potent than the one obtained by the other method.

#### BACTERICIDAL ACTION *in vitro* OF SULPHANILAMIDE AND SULPHAPYRIDINE ON *Mycobacterium lepræ muris*

1. A study has been made of the action *in vitro* of sulphapyridine (M&B 693) and sulphanilamide on the rat-leprosy bacillus.
2. A preliminary experiment suggested that the drugs have a bactericidal action if allowed to act on the bacterial suspension at 37°C. for 48 hours, but that in cold (at 4°C.) they have no such action, even if allowed to act for double the time (96 hours).
3. A suspension of rat-leprosy bacillus was prepared from the tissues of white rats suffering from experimental rat leprosy. This suspension was divided into three portions: one portion was mixed with sulphapyridine to give a dilution of 1/1,000 of the drug; another portion with sulphanilamide in the same dilution; and the third was treated with 5 per cent sulphuric acid and then neutralized. All the three portions were left in an incubator at 37°C. for 48 hours. Injections were then made in three batches of rats.
4. The suspensions treated with two drugs did not produce the disease in the injected animals. The acid-treated suspension produced a generalized rat leprosy. The non-infectivity of the drug-treated suspensions was therefore not caused by the mere storage of the suspension at 37°C. for 48 hours.
5. Thus, sulphapyridine and sulphanilamide, in a dilution of 1/1,000, possess a bactericidal effect *in vitro* on the bacillus of rat leprosy if allowed to act on the organism at 37°C. for 48 hours. Sulphapyridine was found to possess this property in a dilution of 1/10,000 also; results for a similar dilution of sulphanilamide are not available.

#### STUDIES ON THE GLYCOLYTIC BREAKDOWN OF GLUCOSE IN VEAL INFUSION

A rapid and inexpensive method for the production of sarcosolactic acid, by the glycolytic conversion of glucose in muscle infusion, is described.

#### THE EFFECT OF STORAGE ON THE CAROTENE CONTENT OF DEHYDRATED VEGETABLES

1. The effect of storage on the carotene content of six dehydrated vegetables has been studied.
2. The dehydrated vegetables on storage showed a progressive loss in their carotene content.
3. Temperature, within the observed range (18°C. to 37°C.), appeared to have little influence on the rate of destruction of carotene in dehydrated vegetables.
4. The destruction of carotene in vegetables containing a high percentage of chlorophyll was more pronounced in the presence of light.

#### COMBINED ESTIMATION OF THIAMIN AND NICOTINIC ACID IN FOODSTUFFS BY CHEMICAL METHODS

1. A simple, reliable and rapid method has been described, whereby combined estimations of thiamin and nicotinic acid can be made on the same sample. This procedure enables the assay of 5 to 6 foods in a 7-hour day.
2. Hydrolysis at pH 6 to 7 by an enzyme preparation from pig's intestinal mucosa has been employed for the liberation and extraction of thiamin and nicotinic acid. Further, the method has also been found to be effective in reducing the interference by extraneous substances to a minimum.
3. The thiochrome method has been adopted for the estimation of thiamin and the cyanogen-bromide-aniline method for the estimation of nicotinic acid.



4. Various foodstuffs have been assayed for their thiamin and nicotinic acid content and the values obtained were in good agreement with those reported by other workers.

5. Recoveries of added vitamins were satisfactory, ranging from 75 to 100 per cent for thiamin and 83 to 108 per cent for nicotinic acid.

6. In the case of three cereals and one pulse, recoveries of added thiamin ranged from 20 to 60 per cent. An explanation has been offered to account for the low recoveries observed.

7. Autolysis of an aqueous suspension of flesh foods has been found to liberate thiamin and nicotinic acid from their biological combination. However, the use of the enzyme preparation is recommended in order to ensure complete liberation of the vitamins from all types of foods.

#### THE EFFECT OF VITAMIN C ON GINGIVAL AND PERIODONTAL DISEASE IN INDIAN CHILDREN

An experiment was carried out to discover the effect of ascorbic acid on gingivitis and associated conditions in Indian children in an orphanage. One hundred mg. of ascorbic acid was given to 50 children for 100 days, similar control group receiving no supplement. No change in gingival conditions was observed as the result of giving ascorbic acid.

#### THE EFFECT OF 'EXERCISE' ON THE PYRUVIC ACID CONTENT OF NORMAL AND VITAMIN-B<sub>1</sub> DEFICIENT RICE-MOTH LARVÆ (*Corcyra cephalonica* St.)

1. An increase was observed in the pyruvic acid content of normal and thiamin-deficient larvæ, subjected to a period of strenuous 'exercise'. The highest pyruvic acid values were found in larvæ tested three minutes after 'exercise'.

2. The time taken for pyruvic acid values to return to the original level was three hours and was substantially the same in normal and thiamin-deficient larvæ.

#### RIBOFLAVIN AND PYRIDOXIN (VITAMIN B<sub>6</sub>) AS GROWTH-PROMOTING FACTORS FOR RICE-MOTH LARVÆ (*Corcyra cephalonica* St.)

1. The rice-moth larvæ (*Corcyra cephalonica* St.) requires riboflavin and pyridoxin (vitamin B<sub>6</sub>) for its growth. It apparently does not need nicotinic acid and pantothenic acid.

2. The growth of riboflavin-deficient larvæ was proportional to the amount of riboflavin added to the diet up to 1.2 g. per g. of diet. Larger amounts of riboflavin did not accelerate growth.

3. Rice-moth larvæ can be used for the estimation of riboflavin in foodstuffs and biological materials.

#### ACCUMULATION OF PYRUVIC ACID IN RICE-MOTH LARVÆ (*Corcyra cephalonica* St.) FED ON A VITAMIN B<sub>1</sub> DEFICIENT DIET

1. A technique for handling and rearing rice-moth larvæ is described. The larvæ will grow normally on a basal diet consisting of wheat protein, yeast, salt and shark-liver oil.

2. When the larvæ are fed on a vitamin B<sub>1</sub>-deficient diet, they accumulate pyruvic acid like man and laboratory animals. This disappears on the inclusion of the vitamin in the diet.

3. Only a trace of vitamin B<sub>1</sub> is necessary for the promotion and maintenance of growth and preventing the accumulation of pyruvic acid. The larvæ can thus be used for the detection of very small amounts of the vitamin in biological materials.

#### THE RÔLE OF CALCIUM AND VITAMINS IN TUBERCULOSIS : STUDIES ON SERUM CALCIUM IN NORMAL AND TUBERCULOUS SUBJECTS

The serum calcium of 49 healthy and 275 tuberculous men and women living under identical conditions was estimated. It was found that :—

1. The average amount of serum calcium in men is 10.84 mg. and women 10.43 mg. per 100 ml.

2. A significant decrease has been found in the case of men in the early, advanced, active and quiescent

stages of the disease as compared with healthy individuals. However, between early and advanced cases the differences in the averages for serum calcium are not significant in respect of both men and women.

3. No significant decrease has been noticed in tuberculous women patients in different stages of the disease as compared with the healthy state.

4. Hæmoptysis does not seem to affect the level of serum calcium.

#### ON ISOHEMOLYSIS : REPORTS ON TWO ISOLYSINS AND ASSOCIATED CONSIDERATIONS

1. A strong isolysin B was found in a subject O with isonins of equal and middling titre. No anti-isolysins in four subjects B could be detected by its use. It could be reactivated. It could not be separated from the associated isonin. It inhibited hæmagglutination.

2. A weak isolysin A was found in another subject O with isonins of unequal and middling titre. It did not inhibit hæmagglutination. Its reactivation was more limited.

3. Isolysins should disqualify universal donors and donors A and B for subjects AB.

4. Artificially produced hæmolytic amboceptor, isonins and isolysins are compared. Attention is drawn to lack of clarity in observations making high titre isonins responsible for all accidents caused by dangerous universal donors.

#### DETERMINATION OF BLOOD GROUPS FROM STAINS

1. A technique for determining blood groups from stains is described. The *Minimal Dose of Equal and Simultaneous Agglutination* (MDESA) of an equally balanced serum ab is determined. Three such doses contained in 0.1 c.c. dilution of the serum are left in contact with 25 mg. of stained material or 10 mg. of dried blood. After incubation and prolonged contact in the refrigerator the serum dilution is separated and tested for loss of isohæmagglutinins (isonins). Only clear negative and frank positive reactions are accepted. All doubtful cases are excluded from consideration.

2. Remarks on the technique include (i) weight of the dried blood in a stain, (ii) preservation of testing sera, (iii) retardation of agglutination in the final test, (iv) advantages of the absorption test over the extraction and demonstration of isonins, (v) false results and negative results, (vi) rejection of a stain when the unstained control has absorbed isonins, (vii) technique for smaller quantities and for stains other than those of blood, and (viii) a macro-technique *versus* a micro-technique.

3. A photograph gives the essential apparatus and the characteristic macroscopic appearance of the reaction.

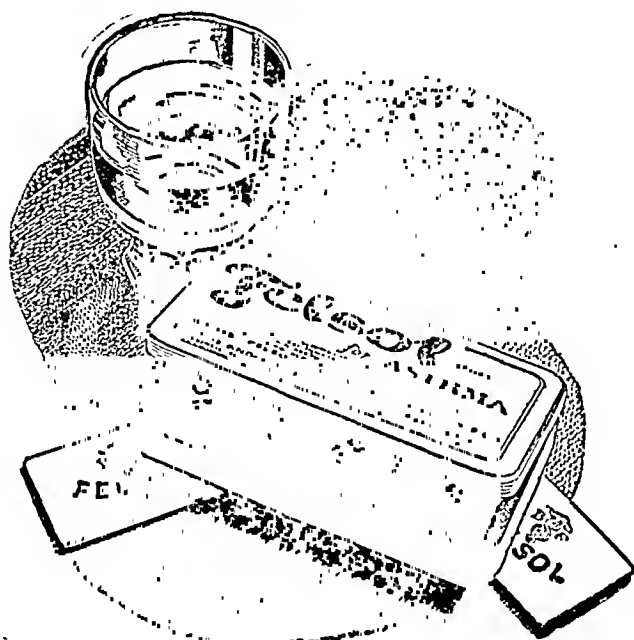
#### STANDARD FOR PAPAIN AND ITS PREPARATIONS

The method of assay of papain activity described in the B.P.C. does not give a true measure of the enzyme activity as the pH of the reaction mixture has been found to be 9.2 while the optimum pH for papain action is 5.0 to 7.0. As the standard is based on this method of assay, the 'standard' as well as the 'method of assay' require modifications.

A modified method of assay suitable for determining the activity of papain is described. This method retains in broad principles the B.P.C. method but the conditions of enzyme action and the quantities of substrate and enzymes suitable for assay have been changed.

The rate of deterioration of samples of papain of various grades of purity, when kept at the temperature of about 25°C. for periods of 3 to 6 months, has been studied. It has been found that the cruder samples of papain retain their activity better than purer samples. The nature of the protective substance in the crude samples of papain is under investigation.

A standard for the activity of papain has been suggested, based on the average activity of papain samples manufactured in India and after making allowance



## THE THERAPY OF ASTHMA

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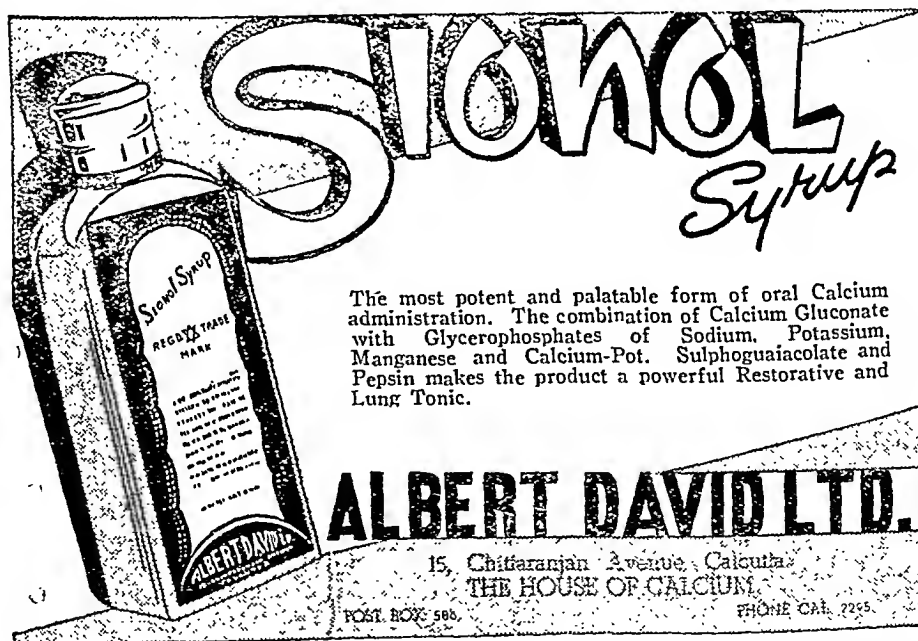
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of about 30 per cent for deterioration. The standard recommended is:—

The amino acids produced by one gramme of papain in the assay process described in the paper should require not less than 25.0 c.c. of N/10 NaOH for neutralization.

The same standard of 25.0 c.c. of N/10 NaOH may be adopted for these following papain preparations:—

1. Elixir papain B.P.C.
2. Glycerinum papain B.P.C.
3. Liquor-papain-*et*-iridine B.P.C.

The quantities of each of the preparations to be added to the substrate in place of papain itself have been calculated and found to be:—

1. 5.0 c.c. adjusted to pH 5 and made up to 10 c.c.
2. 5.6 c.c. adjusted to pH 5 and made up to 10 c.c.
3. 13.5 c.c. adjusted to pH 5 and added to the substrate respectively.

COMPARATIVE PHARMACOLOGY OF THE TOTAL ALKALOIDS OF *Rauwolfia serpentina* BENTH. OBTAINED FROM BENGAL, BIHAR AND DEHRA DUN

1. The total alkaloids obtained from the roots of *Rauwolfia serpentina* Benth. growing in the three different regions of Dehra Dun, Bihar and Bengal, cause a fall of blood pressure. According to the extent and the duration of the hypotensive effect they may be placed in the following descending series: Bihar-Dehra Dun-Bengal.

2. The Dehra Dun root alkaloid has a depressant action which is purely circulatory (central, cardiac and vascular).

3. The Bihar and Bengal root alkaloids have, in addition, slight sedative action on the central nervous system. The Bengal alkaloids have more sedative action than those of Bihar.

4. Respiration is depressed and bronchi dilated by all the three alkaloids.

5. Uterus is stimulated by all, the Bengal variety being the most active while the Bihar variety is the least potent of the three.

6. All the three alkaloids have dual action on the intestine—(i) a preponderating para-sympathomimetic action—stimulation of the intestine annulled by atropine and (ii) a direct slight depressant action. The isolated guinea-pig intestine react always by relaxation.

#### CHOLESTEROL AND HÆMOLYSIS

1. The action of cholesterol on some of the well-known hæmolytic agents, such as the saponins, cobra venom, bile salts and bacterial hæmolysins, has been studied.

2. Cholesterol does not appear to have any considerable retarding action on hæmolysis as was formerly supposed.

3. It retards saponin hæmolysis only when relatively big doses of the substance are employed and when saponin and cholesterol are allowed to remain in contact for some time before the r.b.c. are added. When, however, the saponin is added last there was no retardation whatsoever.

4. It has no appreciable action on cobra venom hæmolysis nor on hæmolysis caused by sodium oleate.

5. Cholesterol retards bile salt hæmolysis in the same way as does lecithin.

6. It has no marked action on either the vibrio hæmolysin (El Tor) or streptococcal hæmolysin.

#### INVESTIGATIONS OF GROUND-WATER POLLUTION, PART I

1. The soil at the experimental site is clayey silt down to 16 feet with sand of medium size below this region. The physical characteristics of the sand were within limits specified by Hazen for applying theoretical formulae.

2. Experiments using sodium chloride as indicator for determining direction of flow of ground water are described. Salt was added to the bore-hole on 3rd June, 1940, and observations on the movement of salt taken till 31st August, 1940. Because of the caving of sand in the central bore-hole there was conspicuous movement of salt in the shallow strata only. The direction of flow in all the three strata lay along well M.J.

3. An experiment for determination of velocity is next described. It was carried out during the season from September 1941 to January 1941, when there was great fluctuation in the water table and slope. No caving occurred during this period and salt flowed freely through all strata. During the height of monsoon the direction of flow swung towards one side momentarily but soon returned to the original direction. The direction of flow of ground water was more or less the same in both experiments.

4. Judging from the rapidity with which salt appeared in the medium and deep wells the velocity of flow during the period might have been as high as 2½ feet per day; there was no significant difference in the velocities in the D and M strata, but in the S stratum the velocity was less than those in the other two strata.

5. Salt flowed from the charging well downwards and to a less extent laterally while water was flowing into the well, diluting the contents at the surface; there was constant proportionate decrease in the salt concentration in the bore-hole. It was estimated that when the water table was 8 feet about one gallon of water per day flowed out of the latrine.

6. There is close correlation between transmission constant of sand samples and the velocity of flow as determined by the field experiment.

7. The significance of the observations in interpreting the flow of

#### Portal Cirrhosis in Iraq

By R. S. STACEY, M.D.

(Abstracted from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. XXXVII, May 1944, p. 387)

1. A DESCRIPTION of the portal cirrhosis of Iraq, based on 1,036 cases, is given.

2. The condition is compared with the portal cirrhosis of western countries. The main differences are in the age incidence, the occupation of the patients, the size of the liver and spleen, the rareness of hæmorrhage and the fact that alcohol plays no part in the ætiology.

3. A positive formol reaction was obtained in 89 per cent of the cases.

4. The serum euglobulin was raised in 95 per cent of the cases.

5. The value and limitations of the formol reaction and serum euglobulin estimation in differential diagnosis are indicated.

6. The ætiology is discussed and the conclusion reached that portal cirrhosis in Iraq is due to a dietetic protein deficiency resulting in a liver less resistant to toxins than normally. The possible sources of such toxins is indicated.

#### Diet and Hepatitis

(From the *Lancet*, i, 8th April, 1944, p. 471)

In his almost forgotten book on geographical and historical pathology, Hirsch attributed an epidemic of jaundice in a Bremen shipyard to (arm-to-arm) vaccination, and supposed that some epidemics of this disease were of a dietetic kind. Anyone reading this twenty years ago would have shrugged his shoulders and reflected that the old observers had some funny ideas. But to-day the first of these premises finds immediate acceptance, while a variety of exact observations focuses attention on the second. It was not until a few years after Hirsch wrote that Weil differentiated the malady which bears his name, and which Inada and his colleagues proved in 1916 to be a leptospiral infection. But one can be sure on clinical grounds that in many of the old recorded epidemics of jaundice the condition was what until recently has been called 'catarrhal jaundice'. The conception of this disease as a duodenal catarrh, associated with a mucus plug in the ampulla of Vater, was one of Virchow's less fortunate contributions to pathology; and like that of his compatriot Koch on the dangers of bovine tuberculosis it had an astonishingly long run

before it was refuted. For it was the biopsy studies of the liver made by Roholm and Iversen in 1939 which established that there is a real hepatic lesion in such cases. An important point in their findings was that in jaundice of various types, excluding obstruction, infection and hæmolytic, a similar picture could be found in the liver. This raised the question whether arsphenamine jaundice, which has hitherto been generally accepted as a simple if capricious toxic effect of the organic arsenical, was in fact of this nature, or whether it fell into line with catarrhal jaundice, undiscovered factors being responsible for its high incidence in venereal diseases clinics.

At this stage war broke out and jaundice soon became a major medical problem. To some extent it was cryptogenic and to some extent associated with known factors. Among these factors were inoculation with a yellow-fever vaccine containing human serum, the use of human convalescent serum for the prevention of mumps, blood-transfusion, and, to bring in some earlier observations, measles prophylaxis with human serum. The general conclusion was that in all of these cases (and here we may hark back to the Bremen shipyard workmen) the important factor was something—possibly a virus—present in human serum which was capable of initiating the hepatic damage. It is also widely accepted now that much 'arsphenamine jaundice' is of the same nature, and conveyed from one person to another by traces of blood left in the syringes used in venereal clinics. The actual pathological changes in the liver in all these conditions are, as far as our present knowledge goes, indistinguishable. In their large series of hepatic biopsies Dible, McMichael and Sherlock were unable to differentiate between the lesions of 'catarrhal', serum, and arsphenamine jaundice. Such studies made during life from the only sure basis for our knowledge of the pathology, for the disease has a low mortality and in fatal cases only extreme changes will be observed, some of which are terminal ones. The essential feature in all these cases is an acute hepatitis, characterized by a necrosis of liver cells and associated with a leucocytic and histiocytic cellular reaction which in milder cases is concentrated in the portal zones; but all degrees of change have been observed from the mild lesions associated with little disturbance of the liver architecture up to the severe lesions in which, if death results, the post-mortem picture is one of acute atrophy, and the late fibrotic lesions in which the picture is one of cirrhosis.

On another page Himsworth and Glynn divide the causes of liver necrosis into a toxic group—in which they would put the cases we have just passed under review—and a dietetic. Many earlier observations had pointed towards the importance of a dietetic influence. Thus Whipple showed that protein deficiency rendered the livers of dogs susceptible to chloroform necrosis, and Earle and Victor found that severe liver necrosis could result in rats from an excess of cystine in the diet. More recently György and Goldblatt, in investigating a dietary deficiency capable of causing an acute focal or diffuse hepatic necrosis with fatty infiltration in young rats, identified the deficient factor as casein. The possibility of counteracting these effects by various dietary supplements was examined, and methionine alone, or cystine and choline in combination, were found to do this. Substantially similar results have been obtained by Himsworth and Glynn, who produced massive hepatic necrosis in rats by a low-protein diet and found that casein, even in small quantities, protected the animals, and, on further analysis, that methionine, and amino-acid in which casein is rich, afforded complete protection. These results clearly prove that dietary factors as distinct from general protoplasmic poisons and viruses, are capable of producing necrosis of the liver in rats. In healing this leads to fibrosis, and if the animal lives long enough to nodular hyperplasia. Himsworth and Glynn differentiate this sequel from portal cirrhosis, which can be produced by diets causing fatty infiltration and also by toxins. On this and other grounds they

describe 'tropho-pathic' and 'toxipathic' hepatitis, with distinctive fibrotic sequelæ, and 'dietary portal cirrhosis'.

The applicability of these differences to hepatitis and hepatic fibrosis in man must await further investigation. The view widely taken by pathologists, and supported as far as man is concerned by biopsy studies, is that the exact histological picture for any agent capable of causing liver necrosis is largely determined by dosage and the duration of the injurious effect. An agent acting intensely may produce acute necrosis and death with the picture of 'acute atrophy', or if survival takes place a picture of fibrosis with a pronounced element of nodular hyperplasia, especially in younger subjects. The same agent acting over a longer period may produce a slightly different picture, such as that typical of alcoholic 'cirrhosis', which it is estimated takes 5 to 15 years to develop. These differences are, however, believed to be differences of degree and not fundamental. To what extent can liver disease in man be attributed to dietary deficiency? While pointing out that 'No certain evidence of the occurrence of massive hepatic necrosis due to a deficient diet has yet been produced' in man, Himsworth and his colleague draw attention to the suggestion that the high incidence of cirrhosis of the liver among poor natives in the Punjab and Rand may be of this nature, a suggestion which Glynn has supported by producing hepatic cirrhosis in rats by feeding them on the ordinary diet of natives in the mines of South Africa.

## Reviews

**STERNAL PUNCTURE: A METHOD OF CLINICAL AND CYTOLOGICAL INVESTIGATION.**—By A. Plney, M.D., M.R.C.P., and J. L. Hamilton-Paton, M.D., M.R.C.S. Second edition. 1943. William Heinemann Medical Books, Limited, London. Pp. xiv plus 69. Illustrated. Price, 15s.

STERNAL puncture has not only made the biopsy study of the bone marrow easy, but has also proved to be a valuable adjunct to diagnosis in certain diseases. Although clinical and peripheral blood findings are sufficient to establish a diagnosis in most cases, the marrow examination gives a more accurate picture and may even throw light on the pathogenesis. The first edition of this book had certain defects; this edition has been revised and enriched by the addition of a number of new plates. The book begins with a brief reference to the primitive cells, gives a normal myelogram, and then proceeds to describe the marrow changes in different diseases of blood-forming tissue. With regard to the illustrations, one would like to know what stain or stains were actually used, and what was the degree of magnification. The last chapter deals with the technique of sternal puncture, describing one method, though other methods are used. There is a figure showing a sternal transfusion apparatus; some information about the method would have been welcome.

R. N. C.

**AIR RAID PRECAUTIONS. MEDICAL MEMORANDUM NUMBERS 2, 3 and 4.** No. 2:—Mobile Medical Units. 1943. Pp. 18. Price, annas 3 or 4d. No. 3:—Organization and Running of the Civil Defence Ambulance Train. 1943. Pp. 16. Price, annas 7 or 8d. and No. 4:—Procedure on the Admission, Transfer, Discharge or Death of Casualties and the Record of Casualties under Government of India War Injuries Scheme, 1943. Pp. 10. Price, annas 2 or 3d. Published by the Manager of Publications, Delhi.

In modern war, civilians are liable to be attacked and killed as well as men in the services; hence medical preparations must take into account the worst that can befall a civil population especially in crowded and industrial cities. It is therefore necessary to keep some plans ready, and with this object the Civil Defence Department of Government of India has issued four

# Prostatic Carcinoma

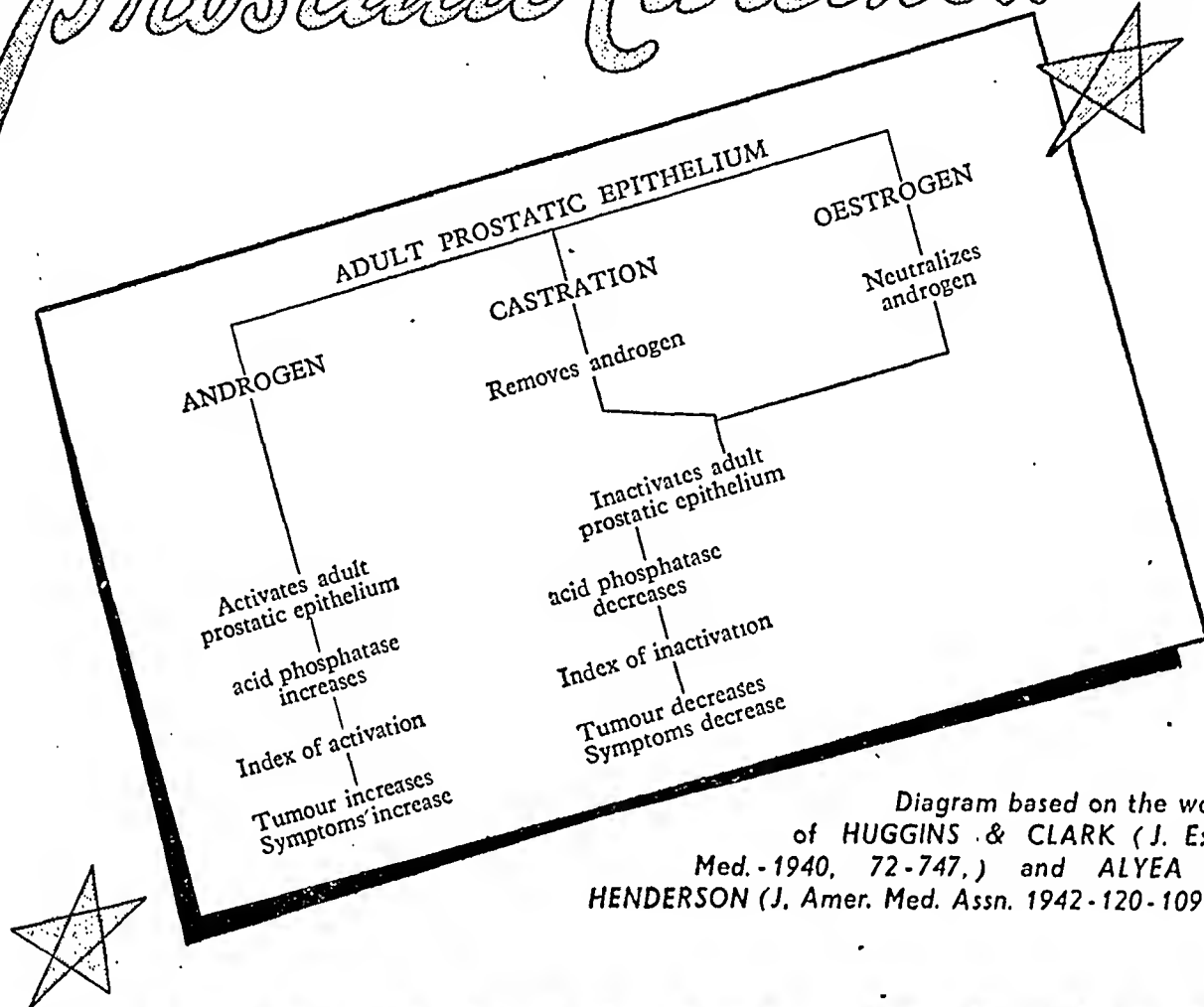


Diagram based on the work  
of HUGGINS & CLARK (J. Exp.  
Med. - 1940, 72-747,) and ALYEA &  
HENDERSON (J. Amer. Med. Assn. 1942-120-1099.)

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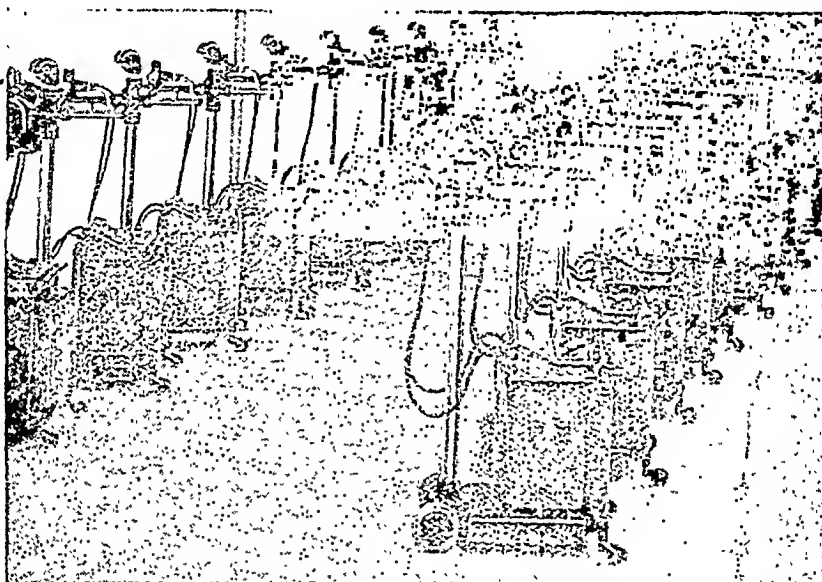
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memoranda on medical organization against air raids for use of doctors engaged in such work. The first one is on *Medical treatment of gas casualties* and has already been reviewed in the *Indian Medical Gazette* of August 1943. Memorandum 2 deals with *Mobile Medical Units* (annus 3 or 4d.) which have a definite rôle in the medical organization of civil defence. They will be mostly required for casualties trapped under debris and urgent cases requiring treatment before removal, and to reinforce a hospital or first aid post which is overworked or which has been destroyed. Memorandum 3 on the *Organization and nursing of the Civil Defence Ambulance train* (annus 7 or 8d.) has been prepared for the guidance of medical officers in charge of such trains as well as those in charge of evacuating or receiving hospitals. Here the work is mostly of an administrative nature. The fourth memorandum deals with the *Procedure on the admission, transfer, discharge or death of casualties and the record of casualties under Government of India War Injuries Scheme* (annus 2 or 3d.) for giving relief in respect of certain personal injuries sustained by 'gainfully occupied' persons, civil defence volunteers and other specified classes, during the continuance of the present hostilities.

R. N. C.

#### PROCEEDINGS OF THE NUTRITION SOCIETY.—

Edited by Dr. S. K. Kon. Published by The Nutrition Society, National Institute for Research in Dairying, Shinfield, Nr. Reading. Price (to non-members) 25s. a year

THIS society was formed in 1941, under the chairmanship of Sir John Orr, with the object of bringing into close association the workers in the fields of human and animal nutrition, for exchange of views and information. It was divided into English and Scottish groups, for the convenience of members during the war. It soon became obvious that the proceedings of the Society should be published and made more widely known, but there were financial and other difficulties, and these have now been overcome with the help of the Royal College of Physicians. The first double number of volume I which has been published contains reports of the first five scientific meetings; these are papers and discussions by research workers and clinicians. For the time being, two double numbers will be published each year.

R. N. C.

#### ABSENCE FROM WORK: PREVENTION OF FATIGUE.—

Issued by the Industrial Health Research Board of the Medical Research Council. Published by His Majesty's Stationery Office, London. Pp. 20. Price, 3d.

THIS pamphlet gives a brief outline of the results of enquiries made in nearly 60 factories by the Industrial Health Research Board of the Medical Research Council in the hope that it may help to explain the causes of unavoidable absence from work, so that steps may be taken to remove those causes.

Illness is the most important cause of absence which increases if the hours of work exceed 60 for men and 55 for women, if there is no week-end break and if the working conditions are bad. Other conditions leading to absence are idle time, wage problem and lack of good feeling between the workers and management.

Although no hard and fast rules can be laid down, since conditions vary so much between one factory and another, it will be well to see that the job suits the person, to avoid too long spells of work, to relay music at intervals, to create interest in the job by explaining what one is working at, and to look after his health. Married women with families should be allowed to do part-time work.

The pamphlet also contains an account of the signs of fatigue and boredom which lead to lowered quantity and quality of work, increased accidents, and discontent and apathy of the workers, with suggestions for their prevention.

R. N. C.

#### BOOKS RECEIVED

1. *Ophthalmic surgery and sight testing*, second edition, by M. A. Kamath. Published by the author (Planters Lane, Mangalore, S. K. Dt.). Price Rs. 6.

2. *Physiological principles in treatment*, eighth edition, by Sir Walter Langdon-Brown and R. Hilton. Published by Baillière, Tindall and Cox, London. Price not stated.

3. *Chest surgery for nurses*, by J. L. Collis. Published by Baillière, Tindall and Cox, London. Price 7s. 6d.

4. *The symptomatic diagnosis and treatment of gynaecological disorders*, by M. M. White. Published by H. K. Lewis and Company, Limited, London. Price 16s.

5. *Aids to materia medica*, third edition, by G. H. News. Published by Baillière, Tindall and Cox, London. Price 5s.

6. *The British encyclopædia of medical practice: Medical Progress 1944*, edited by Sir H. Rolleston. Published by Butterworth and Company (Publishers), Limited, London and The British encyclopædia of medical practice. Cumulative supplement 1944, edited by Sir H. Rolleston. Published by Butterworth and Company (Publishers), Limited, London. Price Rs. 37-8-0 per set of two volumes.

7. *The dental surgeon's handbook: Modern dentistry in daily practice*, by M. Bronner and M. Bronner. Published by John Wright and Sons Limited, London. Price 21s.

8. *Diseases of the nervous system described for practitioners and students*, third edition, by F. M. R. Walshe. Published by E. and S. Livingstone Limited, Edinburgh. Price 15s.

9. *An atlas of the commoner skin diseases*, second edition, by H. C. G. Semon. Published by John Wright and Sons, Bristol. Price not stated.

10. *Textbook of histology for medical students*, third edition, by E. E. Hewer. Published by William Heinemann (Medical Books) Limited, London. Price 17s. 6d.

11. *Textbook of surgical treatment including operative surgery*, second edition, edited by C. F. W. Illingworth. Published by E. and S. Livingstone Limited, Edinburgh. Price 30s. Postage 9d. (Home).

12. *The diabetic A.B.C.: A practical book for patients and nurses*, eighth edition (with war-time supplement), by R. D. Lawrence. Published by H. K. Lewis and Company, Limited, London. Price 4s. and price of the war-time supplement is 9d.

## Abstracts from Reports

### SEVENTEENTH ANNUAL REPORT OF THE SRI RAMAKRISHNA MATH CHARITABLE DISPENSARY, BRODIE'S ROAD, MYLAPORE, MADRAS, FOR THE YEAR 1943

THIS dispensary which was started in 1925 as a side activity of the Sri Ramakrishna Mission treated during 1943 a total number of 73,253 patients of whom 12,906 were new. The report acknowledges the various gifts and contributions received during the year, and appeals for the foundation of an endowment fund and donations in kind or cash for medical appliances and outfits for the dispensary.

### ANNUAL REPORT OF THE KASHMIR MEDICAL MISSION OF THE CHURCH MISSIONARY SOCIETY FOR THE YEAR 1943

THERE were 16,535 new out-patients, and their total attendances were 34,109. The in-patients numbered 2,526 of whom 1,924 were males and 602 females. Three thousand eight hundred and thirteen surgical operations were performed, of these 630 were of major

nature. Six thousand two hundred and seventy-seven laboratory investigations were carried out and 254 persons were x-rayed. The report contains a statement of income and expenditure for the year 1943 together with a list of donations, subscriptions and offertories which amount to nearly Rs. 14,000. The hospital has for nearly three-quarters of a century been a great medical centre for the whole of Kashmir, and from the report before us it appears to be carrying on its good work as in the past.

#### ANNUAL REPORT OF THE PREMANANDA LEPRO DISPENSARY, CALCUTTA, FOR THE YEAR 1943

DURING the year, food crisis interfered with the regular and increased attendance of patients to a great extent, although 757 cases were admitted for treatment at both the clinics of which 582 were at Manicktolla and 175 at Kalighat. Of this number 636 were males, and 161 came from outside Calcutta. The total number of patients was 2,059 and the average daily attendances were 134.5 at Manicktolla and 91.7 at Kalighat. Anti-leprosy injections were given, and the patients also received treatment for ailments other than leprosy such as malaria, dysentery, etc. Kohn test, sedimentation rate and other tests were carried out in the laboratory. One thousand three hundred and twenty-three patients attended sufficiently regularly to justify re-examination at the end of the year. The following results were obtained:—

Diseases arrested—80; much improved—500; slightly improved—465; same as on admission—277; and worse—1.

The home visitor had a very difficult time in tracing the whereabouts of patients who discontinued treatment at their own discretion due to the food crisis in the city.

Mrs. E. David, Lady Superintendent of the Sir John Anderson Health School, sent a batch of girl students to the Manicktolla clinic for training in leprosy. The desirability of training more health visitors in this way is stressed in the report, as it is likely to bring a large number of early cases to treatment.

#### REPORT OF THE SCIENTIFIC ADVISORY BOARD OF THE INDIAN RESEARCH FUND ASSOCIATION FOR THE YEAR 1943

THE annual report for 1943 (Secretariat, New Delhi, price one rupee) contains an account of the researches which were carried out in the various centres. We give below summaries of certain matters and would recommend interested readers to read the original.

**Cholera.**—Sulphanilylguanidine was tried in a series of 174 clinical cholera cases with 1.72 deaths against 6.32 per cent deaths in control cases. It was administered along with other routine treatment, the total dose being 20 gm. The severe cholera epidemic in Madras Presidency in 1943 afforded an opportunity to assess the value of anti-cholera inoculations; it was found that immunity manifested on the fourth day, and the maximum level is reached on the 10th day whilst the protected population is at least 10-times less susceptible than the unprotected in getting cholera.

**Malaria.**—The activities of the Malaria Institute, Delhi, were largely devoted to instructional courses in malariology for officers of the Defence Department. A water soluble stain for rapid diagnosis of malaria has been prepared, yielding very satisfactory results. Certain indigenous drugs were tested on monkey malaria, but found to have no effect on the course of the disease. A spray containing 0.025 per cent pyrethrins has proved effective against flies and mosquitoes, and a vanishing cream containing 0.4 per cent pyrethrins has yielded the most lasting results against mosquitoes.

**Nutrition.**—This is the largest section of the report. Several samples of ghee were tested for vitamin A

content; the average value for pure cow's ghee, obtained from well-fed cows, was 34 I.U. and for pure buffalo ghee only 10 I.U., while ordinary ghee had an average potency of 9 I.U. The heating of ghee at 130°C. for 20 minutes led to the destruction of 45 per cent of the vitamin A originally present. Ghee used in frying puris, etc. was found to lose the vitamin rapidly, and when it is heated to 200°C. or above for more than 10 minutes, practically the whole of the vitamin was destroyed. Dehydrated vegetables cannot be relied upon as anti-scorbutics after a few months' storage. Nutritional diarrhoea is being investigated, preliminary results suggest that injection of nicotinic acid is of considerable value in its treatment. A list is given of those varieties of fish which have been found to be rich sources of one or other of the nutritive constituents. As to the biological value of fish protein, it was found to be the greatest with underdone rather than with raw, fully cooked or fried fish, but in the case of *Hilsa*, greatest value was obtained with fried and least with raw fish. Investigations were carried on the absorption of oils and fats, viz, mustard, coconut, sesame and groundnut oils, margarin, butter fat and vanaspati, and it was found to be high. Their rate of absorption is still under investigation. The presence of fat in the diet was found to increase the utilization of calcium and phosphorus, the most beneficial effect being seen with butter fat; on the other hand coconut oil excites an adverse effect. Experiments on the biological value of soya bean protein and the effect of supplementary value of pulses, when added to a poor rice diet, are proceeding. So far, Bengal gram has shown a slight but definite superiority to other pulses.

There is an account of an enquiry into starvation cases that are admitted into hospitals. The high death rate was due to intercurrent diseases such as malaria, dysentery and pneumonia. The clinical conditions associated with vitamin deficiencies were conspicuous by their absence. Some of the cases died after a few days' stay in the hospital in spite of no obvious disease condition and in spite of nursing, dietetic and medicinal help.

The report also contains accounts of researches in leprosy, plague, pharmacology, maternal mortality and miscellaneous subjects.

#### SUMMARY REPORT OF THE FIFTH MEETING OF THE CENTRAL ADVISORY BOARD OF HEALTH HELD IN NEW DELHI ON THE 4TH, 5TH AND 6TH OCTOBER, 1943

At its fifth meeting in New Delhi in October 1943, under the chairmanship of the Hon'ble Sirdar Sir Jogendra Singh, member-in-charge, the Board considered some important items, one of which was the report of the food adulteration committee. It was obvious from the discussion that the Act was nominally in force; there was unusual delay in disposing of the cases which often ended in condonation of the offences or in imposing penalties where were not deterrent at all. Among its many recommendations were the creation of a cadre of public analysts in each province and state, and the necessity for giving powers to the Director of Public Health to control the working of the Act. In the matter of the post-war planning, the provinces and some of the states appeared to be preparing schemes, but, as Colonels Chopra and Hay pointed out, these depended entirely upon the funds available. Incidentally, Major-General Candy commented on the insufficient staffing of hospitals, whereby a doctor is required to dispose of anything from 300 to 600 out-patients a day; he asked the Board what possible attention a patient could get if he was looked at for a minute. Sir Clutha Mackenzie's report on blindness in India was considered, and the Chairman was requested to appoint a Joint Committee of Health and Education Boards to report on the subject and report on the practicability of his recommendations.

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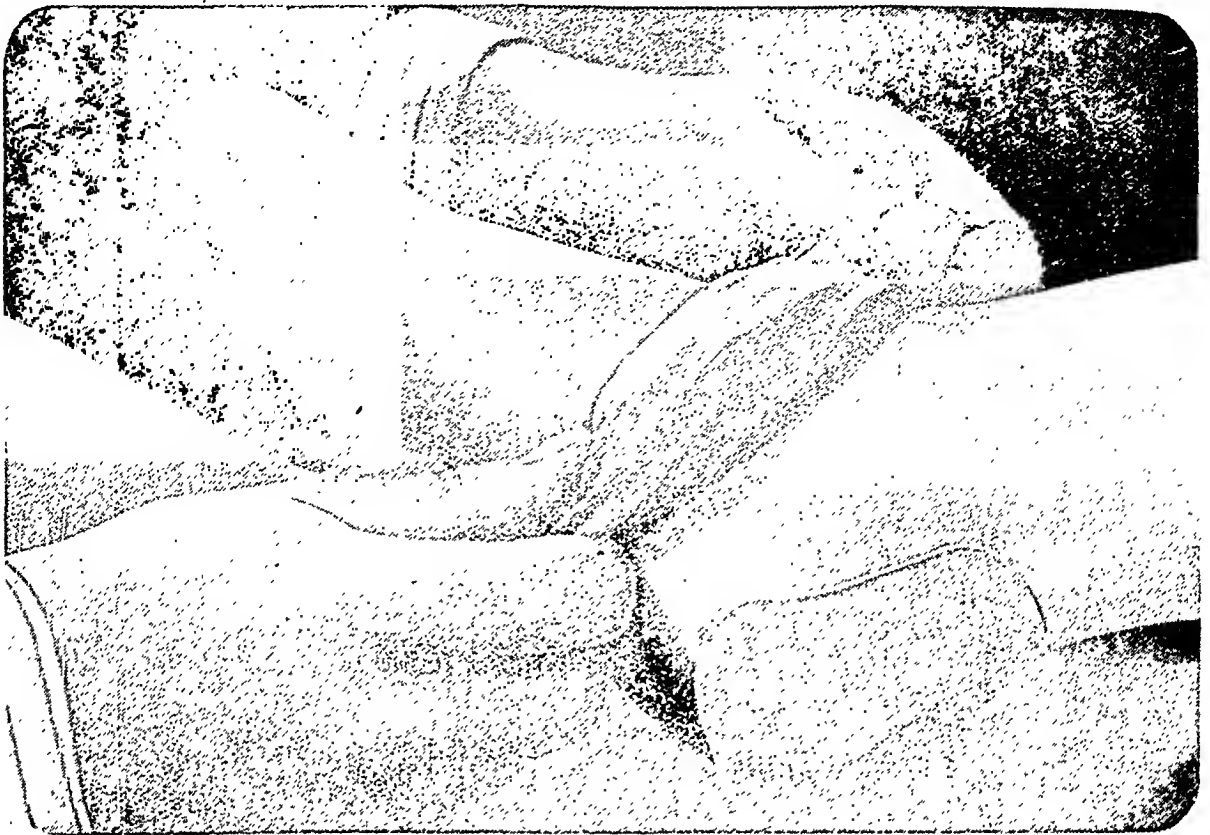
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Dr. B. P. Mazoomdar related his experience of compulsory anti-cholera inoculation at Sitamarhi fair (Behar) in 1942. The Epidemic Diseases Act was introduced with a considerable amount of propaganda but there was at once strong opposition. Various kinds of rumours were spread by mischievous people, and even some of his staff were roughly handled. The number of pilgrims fell from the usual 50,000-70,000 to 25,000, and of these 80 to 85 per cent were inoculated with the happy result that only five suspected cases of cholera occurred during the period of the festival. The experiment was repeated in 1943, when there was usual number of visitors but there was very little opposition. Only 6 cases of cholera occurred and there was no outbreak even after the *mela* was over. Mr. M. C. Desai spoke on the satisfactory control of guinea-worm infection in Baroda State by treating infected wells with lime which destroyed the cyclops harbouring the embryos of the worm. Dr. W. R. Aykroyd gave an idea of the United Nations Conference on food and agriculture held at Hot Springs, U.S.A. Talking about nutrition on which the Conference had laid great emphasis, some speakers said that what India needed just now was quantity rather than quality and that steps should be taken to increase the purchasing power of the masses. One of the final subjects discussed was the acute shortage of nurses all over the country, and the Board recommended the formation of a provincial nursing service.

The Board's function is to discuss and advise on health matters. In many cases, however, it was found that no effect had yet been given by Government to its recommendations passed at the previous four meetings. This is said to be largely owing to the war.

## Correspondence

### SUBSTITUTE FOR CEDAR WOOD OIL FOR OIL IMMERSION WORK

SIR,—Recently while working in the forward area on many an occasion we were short of cedar wood oil. This made me one morning to use castor oil as a substitute, and in my experience it is by far the best, cheapest and easily procurable substitute we can have. Ever since, I have been using castor oil for all my oil immersion work.

D. J. REDDY,  
CAPTAIN, I.M.S.

47 FIELD AMBULANCE;  
6 A.B.P.O.,  
19th August, 1944.

[Note.—The Editor has heard of liquid paraffin being used with good results.]

### MEDICAL EDUCATION IN INDIA

SIR,—May I request you the courtesy of your columns in making a suggestion or two about medical education? Questions of public health have forced themselves on the attention of the highest authorities in the land. In solving these it may be confidently expected that the question of medical education, a very important integral part of the larger question, will be thrashed out well with the help of able and experienced teachers. The improvement of the present standards and the creation of a uniform standard for the whole of India are both very essential.

Three suggestions are made here. Preventive medicine should receive a far more prominent position in the curricula of studies. Post-graduate training (house surgery) extending for a minimum period of one year should be enforced for all new medical graduates before starting any line of work even including preparation for higher courses. Without this, graduation should not be regarded as completed. And as the majority of the medical students in the land

come to the end of their financial resources with the end of their studies, more liberal financial aid during house surgery should be provided for in any plan. A special course in tropical medicine (and preventive medicine) should be made compulsory in all the medical colleges during the period of post-graduate training. Anybody possessing anything like a comprehensive idea of the position occupied by tropical diseases in the larger public health problems of India will readily appreciate this suggestion about the study of tropical diseases.

N. G. PANDALAI, M.D.,  
D.T.M., M.R.C.P.

ANDHIRA MEDICAL COLLEGE,  
MAHARANIPETA P. O.,  
(VIZAGAPATAM),  
9th August, 1944.

## Service Notes

### APPOINTMENTS AND TRANSFERS

THE services of Lieutenant-Colonel K. S. Fitch, Deputy Surgeon-General (Famine Relief Emergency), Bengal, are placed at the disposal of the Government of India for employment as Special Officer in the office of the Public Health Commissioner with the Government of India.

Lieutenant-Colonel R. Linton, Inspector of Hospitals, Dacca, is appointed to be Deputy Surgeon-General (Famine Relief Emergency), Bengal, *vice* Lieutenant-Colonel K. S. Fitch.

Lieutenant-Colonel J. C. De, I.M.S. (Retd.), is, on re-employment, appointed as Inspector of Hospitals, Dacca, *vice* Lieutenant-Colonel R. Linton.

Lieutenant-Colonel J. C. Drummond, on return from leave, is appointed as Civil Surgeon, Hooghly, *vice* Dr. S. C. Sen.

### INDIAN LAND FORCES—INDIAN MEDICAL SERVICE SECONDED TO THE INDIAN ARMY MEDICAL CORPS (Emergency Commissions)

#### To be Captains

Tharamal Vanmeri Narayanan Nambiar. Dated 3rd April, 1943.

Gauri Shankar Nigama. Dated 20th April, 1944.

Gopal Narayan Datar. Dated 14th June, 1944.

Sudhansu Kumar Ganguli. Dated 16th June, 1944.

Joao Francisco Paes. Dated 17th June, 1944.

19th June, 1944

Gopal Narayan Joshi.

Chaganty Sriramachandra Murthi.

Turuvakere Lakshmiramanah Ramakrishna Rao.

Kuduvally Krishna Rao. Dated 28th June, 1944.

Munuswami Subramani Venkatraman. Dated 20th June, 1944.

Arthur Greville Young. Dated 26th April, 1944.

#### To be Lieutenants

Gabriel De Vesselitsky Merriman. Dated 26th April, 1944.

15th May, 1944

Monoj Mohan Roy. Subhendu Ganguli.

Hari Chand. Dated 19th May, 1944.

Madan Lal Barma. Dated 18th June, 1944.

#### AIR BRANCH

The undermentioned I.M.S. officers have been granted emergency commissions:—

#### INDIAN AIR FORCE—MEDICAL BRANCH

##### To be Flight-Lieutenant

Narendra Nath Dutt. Dated 22nd December, 1941.

##### To be Flying Officers

Harjinder Singh Malik. Dated 20th May, 1941.

Mihir Kumar Mitra. Dated 27th April, 1942.

Najmus Saqib Khan (since died). Dated 7th May, 1942.



The undermentioned officer of the I.M.S. (E.C.) reverts from I.A.M.C. and is seconded for service in the Royal Indian Navy :—

Lieutenant G. P. Colaco. Dated 20th July, 1944.

(WOMEN'S BRANCH)

To be Captain

(Mrs.) Maude Elisabeth Khan. Dated 9th May, 1944.

#### PROMOTIONS

Colonel to be Major-General

R. Hay, C.I.E., V.H.S. Dated 17th July, 1944.

Captain to be Major

J. F. A. Forster. Dated 24th June, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Lieutenants to be Captains

E. P. E. Denton. Dated 3rd April, 1944.

M. A. Sirur. Dated 14th June, 1944.

G. Akbar. Dated 30th June, 1944.

1st July, 1944

J. R. Kumar. O. P. Malhotra.

O. P. Khanna. F. A. Shah.

4th July, 1944

N. Khan. J. K. Jindal.

7th July, 1944

S. A. Jafrey. A. T. John.

16th July, 1944

M. F. H. Malik. S. K. Chopra.

M. Latiff. Dated 19th July, 1944.

Z. Ahmad. Dated 31st July, 1944.

9th August, 1944

P. K. Chatterji. H. Chakravarty.

G. P. Ghose. S. C. Datta.

S. K. Sen. A. K. Datta.

B. Banerjee. P. C. Sinha Roy.

J. C. Chatterji. P. K. Chakraborti.

D. K. Roy Choudhury. K. A. Monsur.

M. R. Sarkar.

S. Abedin. Dated 23rd August, 1944.

24th August, 1944

A. K. Ray. S. K. Ray.

Devaprasad Sen. Dated 1st October, 1942.

S. K. Sen. Dated 18th October, 1942.

INDIAN MEDICAL SERVICE

SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY

(Emergency Commissions)

Lieutenants to be Captains

W. S. O'Malley. Dated 17th December, 1943.

J. Chatterjee. Dated 9th August, 1944.

INDIAN MEDICAL SERVICE

SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

(WOMEN'S BRANCH)

Lieutenants to be Captains

(Miss) L. D. Karnick. Dated 29th April, 1944.

(Miss) K. Chaudri. Dated 30th July, 1944.

(Miss) Terway. Dated 11th August, 1944.

INDIAN MEDICAL SERVICE

SECONDED FOR SERVICE WITH THE INDIAN AIR FORCE

(Emergency Commissions)

Lieutenants to be Captains

V. B. Tawadey. Dated 24th January, 1941.

D. N. Gupta. Dated 3rd July, 1944.

4th July, 1944

B. Bhatia. V. B. Kalra.

H. S. Seth.

INDIAN AIR FORCE—MEDICAL BRANCH

Flying Officers to be Flight Lieutenants

H. S. Malik. Dated 15th August, 1941.

M. K. Mitra. Dated 27th August, 1942.

#### RETIREMENTS

Major-General H. Stott, C.I.E., O.B.E. Dated 17th July, 1944.

Lieutenant-Colonel M. Das, M.C. Dated 25th August, 1944.

#### RESIGNATIONS

The undermentioned officers are permitted to resign :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain Constancio Apolinario Rodrigues. Dated 27th July, 1944.

Captain Mukundalal Banerjee. Dated 2nd August, 1944.

#### RELINQUISHMENTS

The undermentioned officers are permitted to relinquish their commissions :—

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captain Dharendra Nath Acharya. Dated 18th April, 1944, on grounds of ill-health.

Captain Inderjit Singh. Dated 12th June, 1944.

Captain Narsingha Chandra Banerjee. Dated 18th July, 1944, on grounds of ill-health and is granted the honorary rank of Captain.

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## Original Articles

STRUMA LYMPHOMATOSA  
(LYMPHADENOID GOITRE :  
HASHIMOTO'S DISEASE)

## A STUDY OF FOUR CASES

By T. BHASKARA MENON, M.D., D.S.C.,  
F.R.C.P. (Lond.)Professor of Pathology, Andhra Medical College  
andF. A. B. SHEPPARD, O.B.E., F.R.C.S.  
MAJOR, I.M.S.Professor of Surgery, Andhra Medical College,  
Vizagapatam

## Introduction

CASES of struma lymphomatosa (Hashimoto's disease) are comparatively infrequent. In 1931 Graham collected only 24 cases from the literature. This figure was brought up to 50 by McClintock and Wright in 1937, and Joll in 1939 added another series of 81 cases. A difficulty has been its differentiation from Riedel's struma, which is still a matter of dispute. So far as we are aware, no cases have as yet been reported in the Indian literature. A study of the following four cases is, therefore, not without interest. Three of these cases are comparatively recent, while one was discovered during a search of the specimens of the Andhra Medical College. The four cases are arranged to show an increasing extent of involvement of the gland.

## Case reports

**Case 1.**—It presents what we have regarded as the earliest phase of the condition.

The patient, a moderately well-nourished woman, aged 40 years, attended hospital on 7th November, 1942, for the treatment of a chronic ulcer of the leg. During examination, it was noted that she had a bilateral thyroid swelling, more marked on the right side where it extended up to the angle of the mandible. The swelling moved with deglutition. The goitre was nodular, and was not adherent to the overlying skin, which was healthy. There was no difficulty in breathing. There were no signs of thyrotoxicosis other than a pulse rate which varied between 94 and 110. The basal metabolic rate was +5.1 per cent. The Wassermann reaction was negative.

On 7th December, 1942, sub-total thyroidectomy, including removal of the isthmus, was performed (F. A. B. S.). The gland, on examination after removal, was solid, lobulated and of a whitish-yellow colour (figure 8, plate XXVI). When cut it showed the same pseudo-lobulation as was noticed on the surface, the consistency was definitely firmer than normal, and no normal amber-coloured thyroid tissue was visible to the naked eye. Vascularity was slight, and the capsular vessels were not engorged (figure 1, plate XXV).

**Case 2.**—The patient was a girl of 14 years, admitted to hospital on 23rd August, 1938, for breathlessness on exertion, and a thyroid tumour of one and a half years' duration. The basal metabolic rate was -18 per cent. Sub-total thyroidectomy was

carried out, leaving only the upper pole of the left lobe (7th September, 1938). During operation it was noted that the gland was enlarged, fleshy, irregularly lobulated, and so firmly adherent to the trachea as to give rise to a suspicion of malignancy. Both lobes of the gland were uniformly enlarged and, with the enlarged isthmus, were almost annular in shape. The general contour was well preserved, but the outer surface showed typical pseudo-lobulation. Blood vessels were prominent in the capsule (figure 7, plate XXVI). On section, the colour was whitish-yellow and the consistency firmer than normal, resembling in general the appearance of a salivary gland. The capsule appeared slightly and irregularly thickened. Trabeculation was slight on the cut surface. There were no areas of degeneration or hæmorrhage, and no trace of normal coloured thyroid tissue was visible (figure 2, plate XXV).

**Case 3.**—A woman of 42 years was admitted to hospital on 6th January, 1932, for goitre. The patient had undergone x-ray treatment elsewhere. On admission, there were pressure symptoms leading to dyspnoea. The patient was sleepy, sluggish and apathetic. The basal metabolic rate was -49.7 per cent. Partial thyroidectomy was carried out on 11th January, 1932. During operation, the isthmus was found to be very wide and firmly fixed. On removal, the gland was found to be diffusely enlarged and the outer surface lobulated.

**Case 4.**—A moderately well-nourished woman of 40 years was admitted to hospital on 27th June, 1942, for carcinoma of the left breast and enlargement of the thyroid. The swelling in the neck had been noticed two months before admission, and had increased steadily to its present size. There was no difficulty in breathing, or in swallowing, and no change in the voice. The thyroid gland was symmetrically enlarged (each lobe 2½ inches by 2 inches), the overlying skin was healthy, and was not adherent to the tumour. No enlarged veins were visible over the tumour, nor was any bruit heard. The tumour was hard, smooth and not nodular. There was no clinical evidence of hyper- or hypothyroidism. Total thyroidectomy was performed on 27th July, 1942, one month after a radical mastectomy for the carcinoma of the breast (F. A. B. S.). At operation, the thyroid was obviously avascular, the capsule on the posterior aspect of the isthmus was thickened, and it was somewhat adherent to the trachea. There was no deformity or distortion of the trachea. On examination after removal, the general enlargement of the lobes and isthmus, noted clinically, was confirmed, and the general contour was well preserved. The capsule was a little thickened and whitish in colour. The consistency was almost cartilaginous. The cut surface had a pale pink colour and a solid cellular appearance somewhat like that of a lymph gland. Here and there, thin strands of white fibrous tissue could be seen. On the whole, there was only faint trabeculation. There were no areas of hæmorrhage, degeneration or necrosis.

## Histology

Case 1 showed the lymphocytic infiltration which is regarded as the typical and most characteristic feature of the condition (Hashimoto, 1912; Joll, 1939), but this was only in focal areas. Such focal areas were, however, widely scattered throughout the gland. Some areas showed the formation of follicles with distinct germ centres and evidence of commencing atrophy of the vesicles and destruction of thyroid tissue. Plasma cell infiltration was slight. Other areas showed more or less normal thyroid tissue, in which the vesicles were of normal size, showed eosinophilic colloid, and were lined with cuboidal epithelium with centrally placed spherical nuclei. Areas showing inspissated colloid were also met with (figure 1, plate XXV). Extreme distension of vesicles, as in colloid goitre, was not found in any part of the gland. With slight distension, the epithelium was somewhat flattened and the nuclei ovoid in shape. Peripheral vacuolation of colloid, indicative of a compensatory activity of the

gland, was very slight. In some areas the vesicles were of a fetal type, lined by high cuboidal epithelium, but with slight hyperchromasia of the nuclei and containing no colloid. There was little distortion of the shape of the vesicles or budding of epithelium, as in Graves' disease. The vascularity was slight. The connective tissue, shown by Van Gieson's stain, was not increased, but was present only in thin bands demarcating large islands of thyroid tissue. The reticulin, as shown by the Foot-Wilder stain, showed no increase.

Case 2 showed marked, diffuse, lymphocytic infiltration. In areas, lymph follicles with germ centres were present. In some places the gland pattern was lost by the cell infiltration. Many of the invading cells were plasmocytes, which had collected in the inter-vesicular spaces and had caused atrophy and distortion of the vessels. Focal clusters of lymphocytes were found, also, in between the lobules in relation to the fibrous septa of the gland. The vesicular epithelium was generally low cuboidal in shape with round central nuclei, and the vesicles showed well-defined eosinophilic colloid. In places, slight peripheral vacuolation of colloid was met with (figure 2, plate XXV), but there was no hyperplastic activity of the epithelium. Areas of atrophy of thyroid tissue were met with, and in places vesicular colloid was invaded by lymphocytes and plasma cells. Symplesmic giant cell formation was not in evidence. The capsule was only slightly thickened, and fibrous invasion of the gland substance was not more than the normal. Staining with Van Gieson, Masson, and Azan stains showed little fibrous tissue between the vesicles. On the other hand, reticulin formation was very marked and appeared in well-defined rings and whorls around each vesicle, with the Foot-Wilder stain.

Case 3 showed complete alteration of the thyroid architecture, and represented an advanced stage of cell infiltration with only scattered areas of fibrosis. There were very few vesicles containing colloid. Most of the vesicles had undergone atrophy and were converted to solid alveoli (figure 6, plate XXVI). The epithelial cells were almost polygonal in type in some areas, and cuboidal in other areas. The nuclei were large, rounded or oval in shape, and some showed distinct hyperchromasia. Mitotic figures were, however, not evident. The epithelial cells appeared compressed and distorted, and symplemic giant cell formation was frequent. This appeared to be due to the pressure effects on the vesicles rather than to an attempt at absorption of colloid as suggested by Joll (1939). Foreign body giant cells, with protoplasmic processes extending into areas of stainable colloid, were not met with. Infiltration, into the vesicles, of lymphocytes and plasma cells was well marked, but the most noticeable feature was the cell infiltration in between the vesicles (figure 3, plate XXV). There were large clusters of plasma cells around shrunken and distorted vesicles looking like the perivascular cuffs seen in syphilitic tissue. Lymphocytes were more marked where lymph follicles appeared. There was comparatively little fibrosis.

Case 4 showed slight thickening of the capsule. Strands of fibrous tissue could be made out spreading into the substance of the gland, and isolating islands of thyroid tissue. The fibrous tissue was thin and delicate in most areas, but more pronounced in others. On the whole, there was a distinct increase as compared with the normal, and this was diffuse throughout the gland. The characteristic feature was the lymphocytic infiltration, which seemed most marked in areas of commencing fibrosis, whilst in areas of dense sclerosis, the lymphoid tissue was aggregated to form follicles, in between strands of collagen. The lymphocytic infiltration was so marked that it formed a cuff of variable density around each thyroid vesicle. In places, the lymphocytes and plasma cells had broken through the wall of the vesicle into the lumen (figure 4, plate XXV). The plasma cell reaction was slight as compared with the lymphoid reaction. Occasionally, lymph follicles with germ centres were met with. The vesicles showed all stages of atrophy and destruction.

There was little colloid formation, so that the size of the vesicle was reduced and the epithelium in places desquamated. In areas of dense lymphocytic infiltration, the acinar structure was lost, and groups of compressed and distorted epithelial cells appeared isolated and surrounded by invading lymphoid tissue. In areas where vesicular structure was preserved, the epithelium was cuboidal in type with vesicular, and occasionally, hyperchromatic nuclei. Symplesmic giant cell formation was infrequent. Distinct necrotic changes were not in evidence, though some of the epithelial cells showed pyknotic nuclei. Reticulin formation by the Foot-Wilder stain, as compared with the normal, was so abundant that each vesicle appeared definitely surrounded by well-defined fibres, and, where the vesicles had undergone atrophy, there were dense whorls of arborizing fibrils.

### Discussion

Significant clinical features of this condition are the appearance in women, usually in the fifth decade of life, of a slowly enlarging, symmetrical or asymmetrical goitre. The goitre is not attended by any ill effects, either local or metabolic, in the early stages. Case 1 and case 2 both presented at the hospital for the treatment of other conditions, and the goitre was not causing any disturbance other than deformity in the appearance of the neck. Later, with increasing suppression of the thyroid tissue and fibrosis, a tendency to sub-thyroidism and pressure effects, such as dyspnoea on exertion, appear. In case 3, where some x-ray therapy had been given elsewhere, the considerably widened isthmus and its adhesion to the trachea gave rise to definite pressure effects, which were relieved by operation. This patient also was 'sub-thyroid'.

The goitre is painless, smooth or faintly nodular, and very firm, even hard, in consistency. There is no adhesion to surrounding structures, and it can be dislocated readily forwards for palpation. The overlying skin remains unchanged. Enlargement of both lobes and the isthmus always occurs, but the size of one lobe may be greater than that of the other, resulting in asymmetry. The trachea is not dislocated but may be compressed in a lateral or an antero-posterior plane.

There has been considerable confusion in the past in differentiating struma lymphomatosa from Riedel's struma. Whilst differences in the age period, the sex incidence, and the clinical features provide wellnigh indisputable evidence that each is a separate and distinct disease entity, differences in the essential pathological features are less distinct. Riedel (1896) described 'eisenhart' goitre as showing microscopically, fibrosis and round-cell infiltration, while in his description of struma lymphomatosa, Hashimoto (1912) described atrophy of the thyroid tissue, lymphoid hyperplasia with the formation of follicles and widespread connective tissue formation as being the essential features. Ewing (1928) regarded both conditions as different stages of the same pathological process, a view which has received considerable support from Vaux (1938). On the other hand, Graham

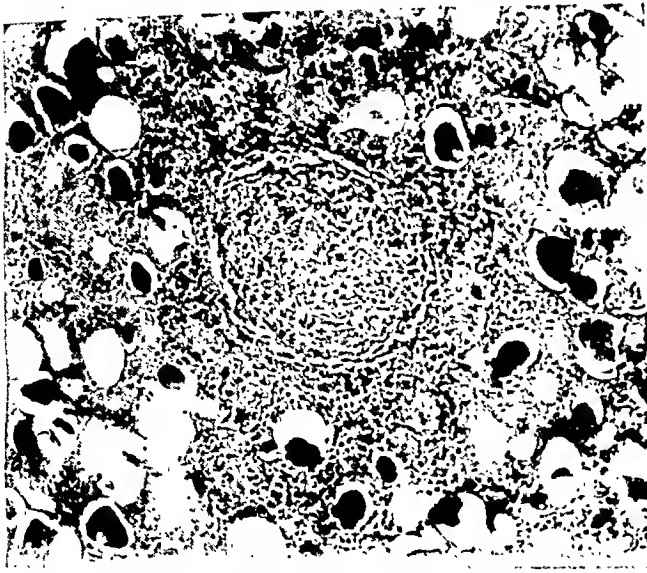


Fig. 1.—Case 1. Showing lymph follicle with germ centre with inspissated colloid in vesicles around. Hæmatoxylin and eosin.  $\times 140$ .



Fig. 2.—Case 2. Showing dense lymphocytic infiltration, atrophy of vesicles, vacuolation of colloid. Hæmatoxylin and eosin.  $\times 140$ .

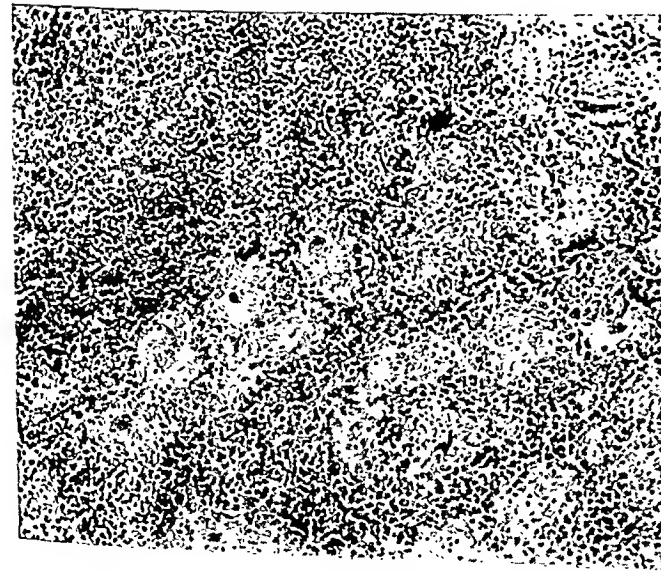


Fig. 3.—Case 3. Showing dense plasma cell infiltration, atrophy of vesicles and absence of colloid. Hæmatoxylin and eosin.  $\times 140$ .

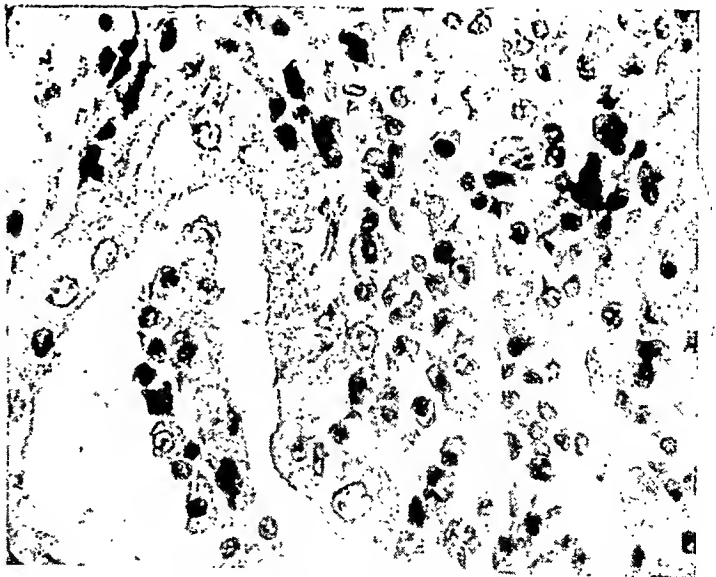


Fig. 4.—Case 4. Showing plasma cell infiltration around and breaking into the vesicle. Hæmatoxylin and eosin.  $\times 660$ .

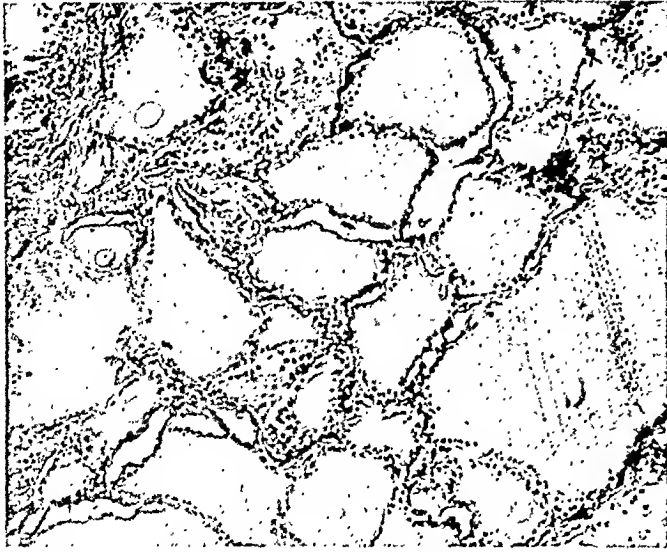


Fig. 5.—Showing delicate reticulin fibres appearing as black lines at the margin of the vesicles in a normal thyroid gland. Foot-Wilder stain.  $\times 140$ .



Fig. 6.—Case 3. Showing branching reticulin fibres appearing as irregular black lines in an area of destruction of vesicles. Foot-Wilder stain.  $\times 140$ .



Fig. 7.—Case 2. Showing an annular type of enlargement, with pseudo-lobulation on the surface. Note the disappearance of colloid on the cut surface.

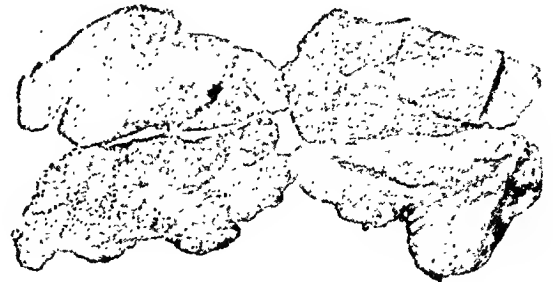


Fig. 8.—Case 1. Showing the slight pseudo-lobulation on the surface and the diffuse nature of the change.



and McCullagh (1931), and more recently, Joll (1939) emphasizing these essential differences, pointed out that whereas Riedel's struma is a localized process of fibrosis of the gland frequently confined to one lobe, and from which extra-capsular adhesions always develop, struma lymphomatosa is a widespread lymphoid reaction which persists without much fibrosis. It is to be noted that in the four cases of this series, the whole gland was involved diffusely, the lymphoid reaction was the predominant feature and that well-marked fibrosis was present only in case 4. These cases, therefore, conform with the condition described as struma lymphomatosa (lymphadenoid goitre). Adhesion to the trachea, in varying degree, was present in cases 2, 3 and 4, but the gland was not adherent elsewhere. Joll has emphasized these points.

To assess the significance of the lymphoid reaction, it must be recognized that similar reactions are met with in Graves' disease, and that, in the atrophied gland of myxoedema, diffuse lymphocytic infiltration and fibrosis are well defined. Collections of lymphocytes are found also in a small proportion of thyroid glands which are otherwise normal. Williamson and Pearse (1929), in their dual theory of thyroid function, regarded the lymphoid reaction as an expression of a special secretory activity of the gland unit, suspended in its peri-follicular lymphatic sheath. If one were to regard the thyroid gland as an organ where the primitive mesenchyme can differentiate into lymphoid tissue as a result of stimuli, the hyperplastic lymphoid reactions and germ centre hyperplasia have features in common with the follicular reticulosis met with in the lymph nodes draining an area of pyogenic infection. In the glands, this would gradually result in an increase of the reticulin fibres and a development of collagen. The significance of the plasma cell reaction has been little stressed. In our small series, it was so marked in case 3 that it overshadowed the lymphoid reaction, and clusters of plasma cells and lymphocytes had invaded the vesicles in cases 2, 3 and 4. While plasma cells are met with in areas of lymphogenesis, extensive plasmacytic reaction and invasion of epithelium suggest a similarity to an inflammatory process. The gradual growth and development of reticulin fibrils, followed by collagenization, also suggest an active process in the primitive mesenchyme of the gland to which the vesicles respond by compensatory activity of the epithelial cells. It is thus possible to regard these four cases as showing varying stages of a pathological process, commencing with lymphoid hyperplasia and germinal hyperplasia, progressing to diffuse lymphocytic and plasmacytic infiltrations with gradual destruction of the vesicular structure, and reticulin and collagen formation. Hellwig (1938) has described a case where, during operative removal of portions of the gland at an interval of nine years, the histological appearances remained

unaltered. But it is difficult to conceive of a similar pathological process which would remain stationary for so long a period. A primary involutionary atrophy of the gland would result in shrinkage, unless there is an over-growth of some specialized tissue which goes on side by side with atrophy of the parenchyma. Hyperchromasia of the nuclei and invasion of the vesicles do not speak for a primary exhaustion atrophy. Simmonds (1923) has suggested lymphogenesis as the cause of the atrophy, and the sequence of changes in this series of cases would support this view.

With regard to the nature of the lymphogenic stimulus, it has been put forward (Feriz, 1933) that products of autolysed epithelium from degenerated vesicles may serve as the chemiotactic factor. On the other hand, the analogy to Graves' disease has suggested that the thyrotropic hormone of the pituitary is the deciding factor (Hellwig, 1938). McCarrison (1929) regards a dietetic factor as causal in experimentally produced lymphadenoid goitre in rats. Whatever may be the special stimulus that is responsible for the lymphogenesis, the sequence of changes and the predominance of plasma cell reaction bring it into line with a chronic inflammatory process, at least in its later stages.

### Summary

Four cases of lymphadenoid goitre are described showing an increasing extent of involvement of the gland. From a histological study, it is suggested that there is a sequence of changes from lymphoid hyperplasia, germinal hyperplasia, diffuse lymphocytic and plasmacytic infiltration with destruction of the vesicular structure, to increased reticulin formation and fibrosis. The tendency to sub-thyroidism is brought out in one case.

Acknowledgment is due to Major F. M. Collins, I.M.S., and Lieut.-Colonel F. J. Anderson, C.I.E., I.M.S., for two of the specimens (from cases 2 and 3 respectively) in the Museum of the Andhra Medical College.

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## STRUMA LYMPHOMATOSA (HASHIMOTO)

### A REPORT OF FIVE CASES

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FIVE cases of struma lymphomatosa corresponding in every essential detail with those reported by Hashimoto have come under our observation, on reviewing 205 biopsy reports of the thyroid in the department of pathology for eleven years ending with December 1943. Since the publication of Riedel's descriptions of struma in 1896, and of Hashimoto's struma lymphomatosa in 1912, there has been much discussion about the origin and nature of these conditions and the possible relationship between the two. Williamson and Pearce in 1929 described a type of chronic thyroid disease—lymphadenoid goitre—which is now considered identical with Hashimoto's disease by almost all writers. A comprehensive reference to various authors who have dealt with this subject up to 1938 is given by Vaux. Most of the writers including Ewing (1940) consider that Hashimoto's struma lymphomatosa and Riedel's struma are different stages of the same pathological condition, the former being the earlier stage. As this peculiar affection of the thyroid is of interest to both the surgeon and the pathologist, there may be enough justification for the publication of a short report of these cases, followed by a brief comment.

**Case 1.**—A Hindu female, Kamalammal, aged 32, was admitted into the General Hospital, Madras, under Dr. B. M. Sundaravadanam on 24th April, 1937, with a diffuse swelling in the front and lower part of the neck of two years' duration, which later led to dysphagia and dyspnoea on bending the neck forward. The goitre increased gradually in size but was unattended either by nervous symptoms or by alteration in the general build indicative of thyroid deficiency. The patient was always active and never suffered from any serious illness, and there was no subjective or objective evidence of hyperthyroidism at any time.

**Physical examination.**—A well-nourished woman; a slightly nodular hard enlargement of the thyroid, especially the right half, moving with deglutition and causing respiratory difficulty and dysphagia; not fixed to the deeper structures; no change in the voice; no eye symptoms or tremors of the hands. Pulse 80, volume and tension fair. B.P. 90/70. B.M.R. not done. Clinical diagnosis—colloid goitre.

**Treatment and operation.**—On 29th April, 1937, under rectal avertin supplemented by nitrous oxide and oxygen, a low collar incision was made in front of the neck, muscles retracted, and the lateral lobes of the thyroid were freed. A big wedge-shaped portion was removed from each of the lateral lobes, and their margins were brought together by continuous catgut. Heavy oozing from the surface vessels which were greatly engorged and tortuous was controlled by catgut ligatures. The skin was closed with a drainage tube.

**Pathological report.**—Only bits of the gland were received for report. Except for a few tiny cystic spaces, the thyroid tissue is solid in consistency. The capsule is thickened and bands of trabeculae are seen dipping into the substance of the gland. Dense bands of fibrous tissue divide the gland into irregular lobules. Diffuse intralobular fibrosis is also evident. The acini are of irregular size, and most of them do not contain any colloid material. The lining epithelium appears to be unaltered. Intra-acinar giant cells are seen in abundance, but there is no evidence of tuberculous infection (see figure 6, plate XXVII). Various stages of formation of these giant cells, from a tiny droplet of colloid to multinucleated foreign body giant cells, are seen. The stroma is diffusely infiltrated with lymphocytes and plasma cells with occasional aggregations of the same in places. Fully formed lymph follicles are not met with.

**Case 2.**—A Hindu female by name Seethamma, aged 34, was admitted into Victoria Caste and Gosha Hospital, Madras, in December 1938 for enlarged thyroid attended with a mild degree of pressure symptoms. Both the lobes of the thyroid were uniformly enlarged. Clinically the case was diagnosed as colloid goitre, and operated on.

**Pathological report.**—One slice of the gland, firm in consistency was received for report. The capsule is irregularly thickened. Thick strands of fibrous tissue intersect the gland. Parenchymal destruction and compensatory regeneration forming solid epithelial masses form a prominent feature. Also large-sized acini distended with deep staining colloid and vesicles lined by columnar epithelium with vacuolated colloid content are noticed. Intra-acinar giant cells are frequent. Diffuse lymphocytic and plasma cell infiltration and localized areas of lymphoid tissue with hyperplastic germinal centres are present throughout.

**Case 3.**—Ragudambi, Hindu female, aged 35, working-class woman, was admitted into the Headquarters Hospital of Masulipatam in April 1940 for a gradually growing tumour of two years' duration in the thyroid region. There was no history of toxic symptoms, and the only clinical symptom reported was a slight degree of sensation of pressure in the neck. During the operation, the gland was found to be hard in consistency, with a thin capsule, and not adherent to the surrounding tissues. The clinical diagnosis was adenofibroma.

**Pathological report.**—Two tiny bits, solid in consistency were received. The capsule is thin and the sectioned surface pale grey in colour. Microscopically the capsule and pericapsular tissues are normal. The gland is divided into small and large irregular lobules separated by strands of fibrous trabeculae of variable thickness. Intra-lobular diffuse fibrosis is also evident. Some of the acini are enlarged, and contain deep staining colloid showing vacuolation in places. Many others are free from colloid, while a few show varying degrees of atrophic change. Intra-acinar giant cell formation is sparse. There is no evidence of epithelial hyperplasia characteristic of toxic goitre. Lymphoid hyperplasia is very marked. Both well-formed lymph follicles with germ centres and diffuse lymphoid tissue are found in the stroma.

**Case 4.**—A married Hindu woman, Sundarammal, aged 30, was admitted under Dr. P. Vadamalayan in Erskin Hospital, Madras, for a goitre which had been present for six years. During the previous six months the goitre had begun to increase in size causing dyspnoea and a sensation of choking. There were no symptoms of toxic thyroid.

**Physical examinations.**—Fairly well-built patient. The thyroid gland was enlarged moderately and the left lobe and the isthmus felt hard. Clinical diagnosis—chronic thyroiditis—probably undergoing malignant change. A subtotal thyroidectomy was done.

**Pathological report.**—Two large-sized bits from either lobes of the thyroid weighing 10 grammes each (figure 1, plate XXVII) were received. They are firm in consistency with sectioned surface uniformly greyish white in colour. No normal thyroid tissue, colloid

material or cysts were recognized grossly. Microscopically the capsule is thickened and infiltrated with round cells (see figure 5, plate XXVII). The glandular parenchyma is irregularly divided into lobules by strands of fibrous tissue. Intra-lobular fibrosis is found extending diffusely isolating even individual cells in places. Parenchymal atrophy and degeneration is more marked in this than in the first case. Epithelial cells showing mitotic figures are occasionally met with. Colloid is scanty. Giant-cell formation and diffuse lymphoid tissue infiltration is similar to case 2.

Subsequent reports indicate that hypothyroid symptoms have become clinically observable, and she has been put on thyroid medication.

*Case 5.*—On 2nd November, 1943, a Hindu female by name Ammakannu, aged 27, was admitted in General Hospital, Madras, under the care of Dr. B. M. Sundaravadanam for a swelling in the neck and difficulty in swallowing for the past six months. The patient was an intelligent woman of average height and weight. She was married 12 years back, had only one child aged nine years, and has not conceived since then. Periods regular with normal flow. She had always been active and had not had any serious illness.

*Physical examination.*—Well-nourished woman without subjective or objective evidence of hyperthyroidism. No evidence of focal infection. No abnormality in the cardiovascular or respiratory system. Temperature, blood pressure, and pulse rate normal. Urine free from sugar and albumin. B.M.R. +23. Local condition—diffuse swelling over the middle and lateral aspects of the neck; moves with deglutition.

*Treatment and operation.*—On 6th November, 1943, under intratracheal ether anaesthesia the thyroid gland was exposed by a collar incision and nearly three-fourths of the gland was resected leaving behind the rest.

*Pathological report.*—The specimen received consisted of the major portion of both lobes of the thyroid (figure 2, plate XXVII). They were much enlarged and coarsely lobulated. The right lobe measures 2 inches vertically,  $1\frac{1}{2}$  inches transversely and  $\frac{3}{4}$  inch antero-posteriorly. The normal contour of the gland is maintained but it is firm in consistency with sectioned surface greyish white in colour. Microscopic appearances are similar to those described in case 3 except that the fibrosis is more marked (see figures 3 and 4, plate XXVII).

#### Summary of five cases

It is significant that all our five cases are in women between the ages of 27 and 35 years. They belong to different districts of the province not known to show many cases of goitre. All of them were married and have conceived once or more. In general, their education was meagre and the social status poor or middle class. The stress and strain of modern life with the attendant emotional disturbances may not have been experienced by them. Varying degrees of enlargement involving the entire thyroid was common in all. The duration of the goitrous condition varied very much. It was six months in case 5 and six years in case 4. The one important symptom which brought them for operation was pressure over the deeper structures adjacent to the thyroid gland, resulting in different degrees of dysphagia or dyspnoea. Symptoms ascribable to hyperthyroidism have been absent in all cases. Symptoms of hypothyroidism were not recorded at the time of operation. Follow-up was possible in only two of the patients, of whom one (case 4) developed

hypothyroid symptoms soon after operation. There is nothing on record to show whether they had any chronic or focal infection.

Malignant change was suspected in case 4, and the rest were clinically diagnosed as colloid or adenomatous goitres. Technical difficulties during operation have not been recorded in any of these cases, evidently because of the absence of adhesions to the surrounding structures.

Macroscopically, we had opportunity to study the major portion of the thyroid gland in two cases and bits from a third case. In these, the capsule was intact and not adherent to overlying structures. The glands were firm and hard and the cut surface uniform and white in colour. No recognizable normal thyroid tissue or colloid material was to be seen. Microscopic findings common to all were atrophic and degenerative change in the epithelium, diminution in the colloid, diffuse fibrosis, hyperplastic germinal centres, extensive diffuse lymphoid infiltration and intra-acinar giant cells. In none of these cases was there any evidence of acute inflammation, tuberculous or syphilitic infection. There was also nothing to suggest neoplasia. We feel that these findings seem to agree with those originally recorded by Hashimoto.

#### Comment

The nature of Hashimoto's disease has long been a matter of discussion. Some of the important questions that have arisen may be reviewed and considered afresh in the light of the cases reported above.

I. Is Hashimoto's disease an earlier stage of Riedel's struma?

Williamson and Pearse (1929), Ewing (1940), Shaw and Smith (1925) and Vaux (1938) contend that Hashimoto's and Riedel's struma are different stages of the same disease, the former being the earlier stage. Other observers such as Joll (1932), Graham and McCullagh (1931) and recently Kearns (1940) disagree from this view. Hashimoto himself has rejected this possibility after careful consideration. The essential features of Hashimoto's disease have been summarized by Graham and McCullagh (1931) as follows: (1) uniform bilateral firm or hard enlargement of the thyroid without notable deformity of the lobes and without definite nodules, (2) close attachment of the trachea without adherence to overlying structures, (3) occurrence in women in middle life or later, (4) absence of symptoms other than those that may be ascribed to moderate compression of the trachea, (5) absence of involvement of regional lymph nodes or evidence of distant metastases, (6) absence of impairment of the general health and (7) absence of signs of local inflammation. To these may be added, the development of myxoedema sooner or later as pointed out by Joll (1932).

Riedel's struma as originally described differs from the above in the following respects: (1)

occurrence in both sexes and at any age, (2) localization to a part of the gland and extension of fibrosis into perithyroid tissue, (3) non-development of thyroid deficiency, (4) histological difference in the nature of fibrosis, this being a dense sclerotic process as against the fine fibrosis seen in Hashimoto's disease.

As many clinical and histological features are common, there have been many attempts to group these two conditions as one progressive lesion, Riedel's struma being considered as a late stage of Hashimoto's disease.

This, however, is not fully justified since (1) it is highly improbable that the later stage of the same disease should occur in younger individuals, (2) there is no available record where, with the help of biopsy, the progressive stages of the disease as described by Shaw and Smith (1925) and later by Vaux (1938) have been substantiated, (3) it is not clear how an initial diffuse lesion should terminate in a localized condition.

II. Is it justifiable to include thyrotoxic cases under the heading of Hashimoto's disease? Histological features such as lymphoid hyperplasia and increased fibrosis are not specific to Hashimoto's disease. Similar changes are seen in endemic goitre, status lymphaticus, and hyperthyroidism. Of these, the changes in the last condition most closely resemble those observed in struma lymphomatosa. The original cases described by Hashimoto and the present group of cases we have chosen to describe were all free from signs and symptoms of thyrotoxicosis. It may be contended that cases of unrecognized hyperthyroidism may pass insidiously into the hypothyroid phase with exhaustion atrophy and fibrosis. But this argument is of no practical importance, since the diagnosis of thyrotoxicosis is made essentially by the presence of detectable toxic features. Also if Hashimoto's disease is a later stage of toxic goitre, the incidence of the former should be greater than the percentage recorded in literature. It would seem, therefore, that cases with previous toxic features should not be mixed up with pure cases of Hashimoto's disease solely because of histological similarity, as has been done by Vaux and other authors.

#### *Etiology and pathogenesis*

The etiology and the pathogenesis of this condition still remain obscure. Chronic inflammation, specific granulomatous conditions, involutionary processes and constitutional disorders have been suggested from time to time by several workers. Hellwig (1938) suggests that it is the result of a functional disorder where the cycle of colloid storage and release is fundamentally disturbed due probably to an excess of thyrotropic hormone, but convincing experimental or clinical evidence is lacking. The clinical histories of our cases reported do not point to any particular etiological factor.

#### *Summary and conclusions*

1. Five cases of Hashimoto's disease are reported.
2. Differences between Hashimoto's disease and Riedel's struma are pointed out.
3. It is contended that cases with a history of toxic features should not be included in this category.
4. Since the natural course of the disease is to end in hypothyroidism, complete removal of the gland ought to be avoided by a preliminary biopsy in suspected cases.

Our thanks are due to the various surgeons who have sent us the biopsy specimens and the superintendents of the respective hospitals, who have permitted us to make use of the case records.

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### EPITHELIOMAS OF THE PALATE CAUSED BY SMOKING OF CIGARS WITH THE LIGHTED END INSIDE THE MOUTH

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EPITHELIOMAS of the mouth are common, and they are generally found on the lips, on the tongue, on the alveolar margin, on the cheek, on the fauces and on the palate.

A statistical record of 335 cases (Kini and Rao, 1937) shows the incidence of this type of growth in different anatomical situations:—

Alveolar margin and jaw	..	13
Cheek	..	26
Fauces and pharynx	..	14
Palate	..	52
Tongue	..	50

Cancer of the cheek and of the alveolar margin is a common experience in Southern India where betel chewing with or without tobacco is common. West Coast of India, specially Malabar, provides the largest number of such cases. It is difficult to say the proportion of cases that occur among those who chew with tobacco and those who chew without it, as specifically recorded evidence is meagre. The constant habit of keeping the 'quid' is a noticeable feature. It is more common among those

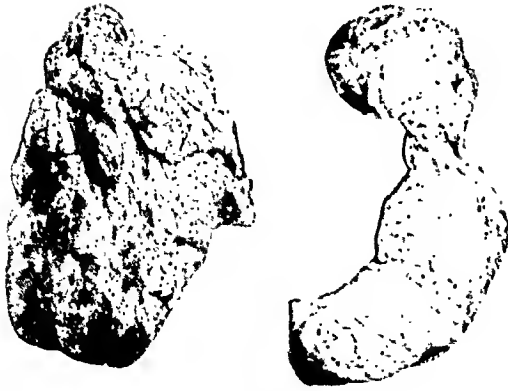


Fig. 1.—External surface of the right lobe and cut surface of the left.



Fig. 2.—External surface of the right lobe and cut surface of the left. Note the coarse lobulation but smooth surface.

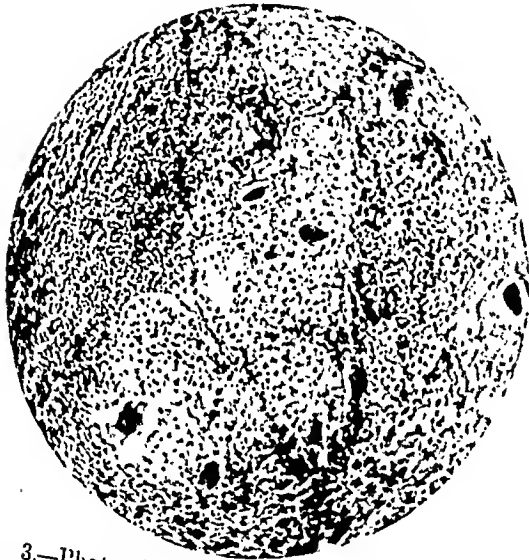


Fig. 3.—Photomicrograph. Note the solid islands of epithelial cells without definite acinar formation, surrounded by extensive lymphoid tissue (case 5).



Fig. 4.—Photomicrograph. Another field from case 5 to show intra-acinar lymphocytic infiltration to the right, and hyperplastic lymphoid tissue to the left, with a wavy band of fibrous tissue in between.



Fig. 5.—Photomicrograph. A field from case 4 to show perilobular fibrosis and diffuse lymphocytic infiltration.



Fig. 6.—Photomicrograph. A field from case 1 to show intra-acinar giant cells.



Fig. 1.



Fig. 2.



Fig. 3.



Fig. 4.



Fig. 5.



Fig. 6.



Fig. 7.





who chew tobacco and less commonly found among those who chew without tobacco. An unhealthy condition of the gum margin with pyorrhea alveolaris is a constant noticeable factor.

Bradfield experimented in lower animals by irritating the cheeks with *chunam* used with betel leaves and also betel nuts on the supposition that it was an irritation cancer, with no noticeable effect. Orr and Sommerville have observed that the habit of retaining the quid of betel and tobacco in the cheek may be responsible for the irritation and believe that there is a carcinogenic factor in the tobacco. This carcinogenic factor has not so far been isolated.

It is difficult to assess the changes that take place in the tobacco that is chewed. A large amount of biochemical and biological investigation has to be undertaken to determine the chemical changes that take place in order to evaluate the existence of the carcinogenic factor like that found in coal-tar derivatives. In smokers of tobacco, it may require investigation to find out if it is the heat of the lighted cigar or the hydrocarbon in the smoke that is responsible for the causation of cancer. It is not unlikely, however, that in view of the large incidence of cancer among betel chewers and smokers of tobacco, there may be a possibility of a carcinogenic factor responsible for the production of cancerous condition in this region.

The average age incidence is usually in the fourth decade or after in all these cases.

While cancer of the cheek and alveolar margin is common in the West Coast, cancer of the palate has been found to be common in the Northern Circars. An inquiry into the incidence of this type of cancer showed that there was a peculiar type of smoking with the lighted end inside the mouth (see figures 1 and 2, plate XXVIII). This habit usually starts from a very young age. Children of 6 and 7 years begin to acquire this habit and continue it throughout their lives. No satisfactory explanation could be obtained from the individuals for this habit of smoking with the lighted end inside the mouth. Some merely stated that it was a habit with them, and it gave them comfort while working. The heat of the lighted ends inside the mouth causes irritation and bears similarity to the irritation that is produced round the naval in Kashmir described by Neve (1924). Cancer of this type usually begins to manifest itself after the age of 30, the average age being 42.5 years. The oldest case in the series was 60 years. As a result of the irritation produced by the heat, changes occur in the epithelial lining of the palate, this undergoing leucoplakic changes at the site where the lighted end lies in juxtaposition (see figure 3, plate XXVIII). They seek advice when one of these patches begin to bleed or smart while eating curry stuff. Sometimes either due to burns or irritation, they develop ulcers which vary in shape and size (see figures 4 and 5, plate XXVIII). The ulcers

may be irregularly oval or crescentic, and usually smart especially when they eat curry stuff. These ulcers undergo a malignant change, and when they do so, they are either of the nodular type or of the ulcerative type (see figures 6, 7, 8 and 9, plate XXVIII).

On histo-pathological examination, they have proved to be true epitheliomas of the squamous type. The secondaries usually spread to the lymphatic glands in the sub-maxillary area and later to the upper anterior superficial and deeper cervical group of glands (see figure 10, plate XXVIII).

### Treatment

Whenever patients reported with leucoplakic patches or with small bleeding ulcers in the palate, they all reacted to simple rules or oral hygiene and dietetic treatment with complete stoppage of smoking. Propaganda conducted among the population of the hospital to avoid smoking with the lighted end inside the mouth proved useful in preventing the development of malignant changes in cases where the ulcer was recent and small. Diathermy coagulation was useful in stopping bleeding from the ulcers and in healing them. For malignant ulcers limited to the arch of the palate and not extending to the alveolar margins with no secondaries in the lymphatic glands, radium plaque application in Stent's composition gave immediate beneficial results. Diathermy coagulation was also tried with indifferent results. As deep x-ray was not available, this could not be tried to evaluate the line of treatment. Operative interference for this condition due to anatomical difficulties was considered inadvisable.

### Points of interest

- (1) This type of cancer is reported to show the peculiar contributory factor in the production of cancer of the palate.
- (2) It becomes evident from the recorded evidence that it takes a long time for the cancer to develop.
- (3) It is difficult to state definitely without experimental evidence whether there is a carcinogenic factor responsible for this condition.

### EXPLANATION OF PLATE XXVIII

- Fig. 1.—Shows the woman adjusting the lighted end inside the mouth.
- Fig. 2.—Shows the cigar in position.
- Fig. 3.—Shows small leucoplakic patches on the hard palate, particularly in the midline.
- Fig. 4.—Shows ulceration which is crescentic in shape situated more towards the left of the palate.
- Fig. 5.—Shows an irregularly oval ulcer in the centre of the palate.
- Figs. 6 to 9.—Show the various clinical types of malignant growths on the palate.
- Fig. 10.—Illustrates the situation of secondary involvement of glands.



(4) Deep x-rays from a Chowla's tube may prove beneficial but has not been tried as deep x-ray of any type was not available.

(5) A follow-up has not been possible due to difficulties in getting replies to enquiries.

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### ŒDEMA AND SCABIES IN A FAMINE HOSPITAL

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#### œDEMA

THESE cases formed a large majority of the total admissions. Amongst them the death rate was particularly high, one out of each seven admissions not leaving the hospital alive. The observations that follow are based on over 300 cases of œdema admitted.

It is a remarkable fact that seldom was there available a history of true starvation; nor was a single case of true beriberi seen, whether inside the hospital or in the outpatients' department. Some cases showed 'dys-sebacia' and phrynoderma as a minor evidence of vitamin B or vitamin A deficiency, but more gross signs of avitaminosis such as cheilosis, glossitis, photophobia with corneal vascularization or pellagra were rare. A few cases, however, did have spongy gums and scattered areas of subcutaneous hæmorrhage.

In the absence of laboratory facilities, it is not possible to be sure of the true ætiology of these cases. Clinically, they roughly fell into the following sub-groups:—

	Per cent
(a) Œdema following malaria ..	20
(b) Œdema following bowel upset ..	25
(c) Subacute nephritis ..	7
(d) Lipoid nephrosis ..	1
(e) Portal cirrhosis ..	3
(f) Anæmia ..	8
(g) Chronic heart failure ..	1
(h) Other causes ..	35

#### (a) Œdema following malaria

People of all ages were affected. There was a history of low-grade pyrexia of several months' duration, but for the last fortnight or so there had been a gradual onset of œdema of the feet and legs. Splenic enlargement was present, and also a moderate degree of anæmia and emaciation. The bowel action was usually normal, and the urine was clear with only a trace of albumin.

These patients gave very little trouble and did well on rest and a course of quinine and ferrous sulphate. They were kept on ordinary diet. The more severe cases of this series were given postural treatment in addition by raising

the foot end of the bed. Their average stay in hospital was about a week, after which they were usually sent to a convalescent home for feeding up.

#### (b) Œdema following bowel upset

Usually there was a history of passing blood and mucus some months previously, and although this had got better within a couple of weeks, the bowels had never been quite normal since. There had been attacks of diarrhœa alternating with constipation. At the time of admission, œdema of the lower extremities was usual and of about a week's duration. The main complaint, however, was of incessant diarrhœa and marked debility. The stools were invariably watery with only a small amount of fæcal matter and bile. There was never any vomiting.

This group was the cause of a very high rate of mortality, about 25 per cent dying, no matter how enthusiastic the treatment. Glucose-saline was invariably administered intravenously in copious amounts, and large quantities of kaolin and glucose were given by mouth. Sulphaguanidine (or sulphapyridine) appeared to do good in cases with a definite history of dysentery, although no blood or mucus was at the time discerned in the stools. Quinine was often used in cases showing splenic enlargement but with doubtful benefit. Vitamin B<sub>1</sub> (and in later cases vitamin B compound tablets) was given to most cases as a matter of routine, but I doubt whether it did any good at all.

*Protein hydrolysates.*—At this stage, I may mention the use of glucose-peptone. It was certainly a life-saving measure in at least some of these cases. With such profuse diarrhœa feeding of these patients was a problem. Rice water with plenty of glucose and common salt was given, but in the stage of inanition in which most of them were, on account of prolonged purgation, the quantity they took by mouth was hopelessly inadequate. Orange juice and citrated milk were also tried, but in Bengal it appears that there is an intrinsic distaste for milk. Glucose-peptone solution (protein hydrolysates) as supplied by the All-India Institute of Hygiene, Calcutta, was often tried, and I think it pulled round some of the patients who were, according to previous experience, considered hopeless. In very few cases was there any severe reaction; only two or three patients died with a rigor about three hours after an intravenous administration of the hydrolysates. To patients who showed improvement, up to 600 c.cm. were given in three doses of 200 c.cm. each, at an interval of 5 or 6 hours. In these cases improvement was often rapid, and even the diarrhœa somehow came under control within the next couple of days (was this due to vitamin B?). During this period peptone administration was continued till the patient could be safely put on more substantial diet such as milk or even rice. Needless to say,

kaolin was also invariably given by mouth to all these cases.

*Technique.*—I have come across some medical officers who have been working in other famine relief hospitals, and it appears that none of them are conversant with the right technique of the use of the protein hydrolysate set (Haye's pattern) as supplied by the All-India Institute of Hygiene, Calcutta. The technique described in the *Indian Medical Gazette* of

I was using the metal cannula, not for intravenous purposes, but for performing paracentesis abdominis in cases of respiratory distress from large ascites.

(iii) Keep an eye at the bubbles moving up through the needle (C). Should the bubbling stop it is almost a certainty that the needle (G) is no longer inside the vein. This often

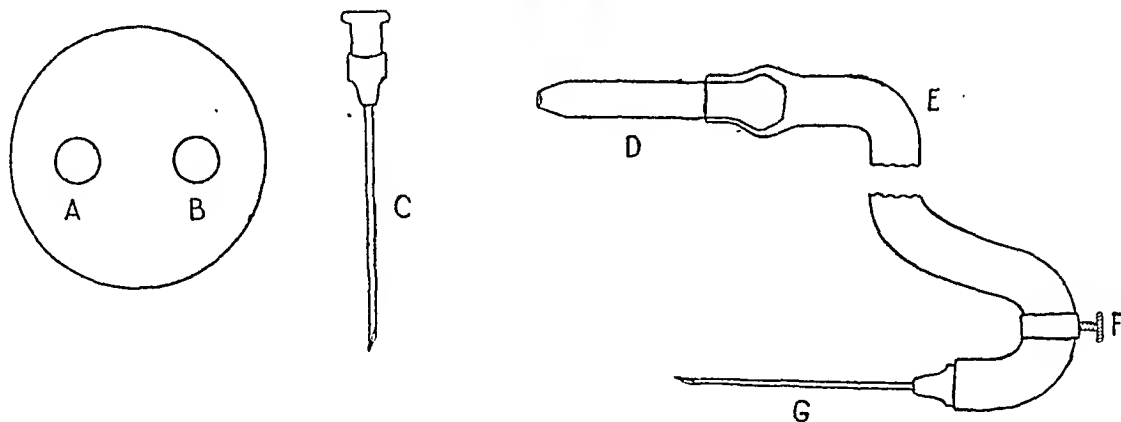


Fig. 1.

February 1944 in the article on 'Treatment and Management of Starving Sick Destitutes' by the committee of the Indian Research Fund Association can be improved upon by using the following method (see figures 1 and 2).

On removing the paper wrapper from the mouth of the bottle two holes (A and B) at once come into view in the tin lid. The rubber membrane stretching across under the lid will be seen sucked in towards the inside of the bottle. With a swab of tincture of iodine completely wipe the surface of the lid and of the membrane. A very fine bore hypodermic needle (C) is then pushed in through the membrane at hole (A). There will be a roar of suction of air and the rubber membrane will soon be seen to rise up close to the tin lid. Next, sterilize over a flame one of the points of a pair of scissors (or any other sharp instrument). Push it through the hole (B) so as to pierce the rubber underneath. Withdraw the scissors. Now the glass cannula (D) is pushed through this hole. Stop-cock (F) is put into position and the far end of the rubber tubing (E) is connected to another fine hypodermic needle (G). The bottle is now suspended upside down. Stop-cock (F) is opened. The fluid at once starts flowing through the tube and bubbles of air are seen passing through the needle (C) into the bottle to replace this fluid. By raising and lowering the tube (E) all air bubbles are removed from the length of the tube. The height of the bottle is now adjusted to allow roughly 60 drops of fluid per minute to flow through needle (G). The set is now ready for intravenous use. Needless to mention all the accessories are previously sterilized by boiling.

As soon as the needle (G) has been introduced into the vein bubbles of air will start passing upwards through needle (C). If it does not so happen, then either one of the needles is blocked or you are not inside the vein.

#### Special points

(i) Needle (C) must be fine. One of large bore will not work, and the fluid will keep on dripping through it.

(ii) Large cannulae supplied in the transfusion set are useless and are not to be used. They are far too large in size to push into a vein.

happens when the patient is very restless and is flinging his limbs about.

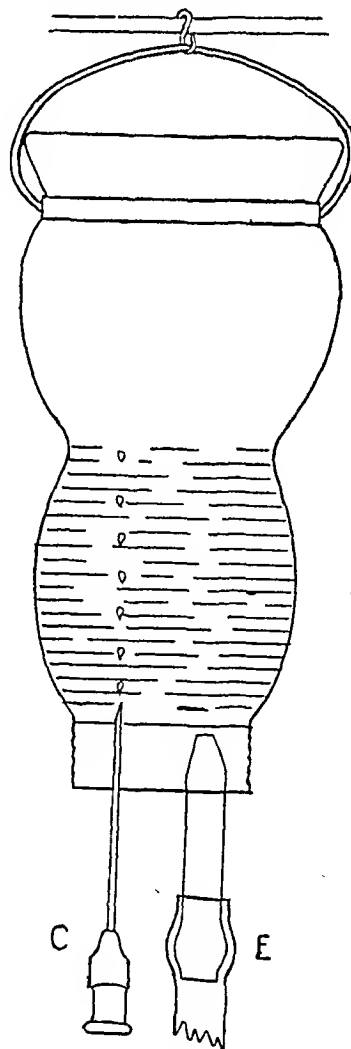


Fig. 2.

It will be seen that no extra complicated apparatus is required. With the sets previously sterilized it has taken me less than 5 minutes to get the fluid running into the vein, starting from scratch.

Essential oils (cholera mixture) were also tried in a few cases but the result was disappointing. It put the patients right off taking any fluids by mouth and in a few instances gave rise to actual vomiting.

#### (c) *Subacute nephritis*

Cases were typical with a recent history of anuria or slight hæmaturia. Since then, a general œdema of the body, eyelids, and sacrum had gradually developed. These cases usually improved on potassium citrate and sodium bicarbonate mixture with restrictions of salt and fluid intake.

#### (d) *Lipoid nephrosis*

This was an interesting group. All cases ranged between the ages of 3 and 16. There was an enormous œdema of the whole body with a very large degree of ascites. One child of 13 had an abdominal girth of 40 inches which after a month of treatment in hospital gradually subsided to 21 inches. It was a common sight to see the skin on the dorsum of the feet, scrotum or the penis sloughing off from distension. In all these cases the urine was scanty and full of albumin. Mucous membranes were pale. Blood pressure (systolic) was invariably below 100 mm. Hg. There was no complaint of visual disturbances.

The treatment of these cases was particularly gratifying. Practically all improved on intravenous protein hydrolysates. The explanation is obvious. It was a simple case of replacing the proteins in the blood which had been lost in the urine.

In these cases salt was restricted, and complete rest was advocated. Residual œdema took a long time (3 weeks or more) to clear and was greatly assisted by oral administration of theocin sodium acetate in the usual doses. Administration of iron and liver extract was later useful in putting up the hæmoglobin.

It may be mentioned that the child with an abdominal girth of 40 inches had to be tapped immediately on admission as he was suffering from acute respiratory distress.

#### (e) *Portal cirrhosis*

All these cases were men. Their ages ranged between 30 and 55. Practically all had massive ascites with respiratory distress. Besides they also had œdema of the lower extremities (from cardiac embarrassment?). They were all brought to hospital on stretchers.

In each case the œdema, though of gradual onset, had been present for months. One of the cases was in his second attack, having recovered from the first about a year previously.

All these patients had to be tapped, and a maximum amount of ascitic fluid removed. They

were immediately put on ammonium chloride and neptal (1 c.cm.) given intravenously. Initial improvement was rapid following a marked diuresis, but at least two such patients never got quite free from their ascites after treatment lasting for over a month.

#### (f) and (g) *Anæmia and chronic heart failure*

These cases were easily recognized. The cases of chronic heart failure were evidently those following hyperpiesia. Only two of the latter group were admitted, one died on the third day during an attack of cardiac asthma followed by acute œdema of the lungs. It is a pity that neptal was not available in those days because he appeared to be a case who might have improved with this diuretic at an early stage. The other case absconded.

#### (h) *Other causes*

This group is rather difficult to analyse. Although it formed nearly a third of the total percentage, it was difficult to fit it into any of the sub-groups mentioned above. Some of the patients presented themselves with rather a solid œdema of the feet along with œdema of other parts of the body. Prolonged rest and nourishing diet had a beneficial effect, but the improvement was very slow as compared to other cases where the cause was more or less known. Prolonged treatment with neptal was very successful, but complete disappearance of œdema would not occur at least in some of the cases.

It was only in this sub-group that any evidence of avitaminosis was found. Apart from dryness of skin, some of them had dermatitis akin to pellagra. Bowel disturbances were frequent. They, in most cases, reacted to vitamin medication.

Some patients had cardiac hæmic murmurs but no actual evidence of valvular incompetence. The heart often showed signs of dilatation, but the blood pressure was never suggestive of hyperpiesis. The liver too was not invariably enlarged or tender. They were possibly cases of acute beriberi without any nervous manifestation. The death rate among these was again very high. In many such instances the pericardial sac was aspirated post mortem but never was there found any evidence of excessive fluid.

Two patients with marked œdema and splenic enlargement, and running a low-grade pyrexia, were not showing any improvement with quinine. Both of them reacted favourably to urea-stibamine injections.

One patient with marked anasarca, intermittent pyrexia, tachycardia, hepatic enlargement and tenderness, and palpable spleen showed no sign of improvement for over three weeks. She was eventually put on emetine. She recovered.

It would thus appear that this group was composed of miscellaneous causes. Some of the

cases were probably atypical types of the preceding sub-groups, and some perhaps had their origin in various combinations of these sub-groups. Quite a number of them with symptoms of diarrhoea were probably cases of vitamin B deficiency in addition to other factors.

*Diet.*—A word may be said at this stage regarding special dietary adopted. Most cases of œdema were given a generous diet including milk, raw eggs, and citrus fruit. This applied in particular to cases of lipoid nephrosis. Cases with anuria were kept on milk and rice only, plus any fruit that was available. Cases with marked diarrhoea were maintained entirely on fluids till their condition started to show slight improvement in that direction.

*Discussion.*—Subacute nephritis, lipoid nephrosis, portal cirrhosis, anaemia, and chronic heart failure as causes of various types of œdema require no introduction. But what about the sub-groups *a*, *b*, and *h*?

Malaria, especially quartan, has long been known to give rise to nephritic manifestations, but I am not aware whether the quartan type of malaria is common in Bengal, indeed if it occurs at all. In any case, these patients did not show any nephritic symptoms. Malaria by itself as a cause must therefore be ruled out. To my mind there is one common feature to all those three sub-groups (*a*, *b*, and *h*). In each instance the patient has suffered from fevers, or diarrhoea, or avitaminosis. All, or any of these factors, operating for a prolonged period, are bound to sap one's vitality ending in loss of appetite and general emaciation. It may also be remembered that this epidemic of œdema has only victimized the very poor who had but little funds to afford treatment at an early stage (even if quinine had been available in the market) and whose larder was equipped with the barest necessities of food, leaving out of consideration all luxury foodstuffs. It is conceivable, therefore, that their œdema was really caused by inadequate supply of food which was poor in first-class proteins, and often in vitamins as well. It is true that none of the patients actually admitted starvation, but from the above it is reasonable to consider the origin of œdema as really lying in true inanition. I am not aware whether œdema has ever been observed among professional fasters, but such people have usually had a good reserve of proteins and vitamins before they ever commenced a fast. Besides they usually did not absolutely deprive themselves of vitamins, etc., even during the course of the fast. In any case their fast did not perhaps last long enough for any of the deficiencies to show themselves in the form of œdema.

I am aware that a lot of laboratory work has been going on for some time to find out if the blood actually shows any deficiencies in its total proteins in such cases. I understand that such is the case in nearly 50 per cent of all cases of œdema. The result of estimation of

other blood constituents will also be awaited with great interest.

*Causes of death.*—As usual, children and old people produced the highest mortality. Cases with marked diarrhoea just sank gradually; their blood pressure continuing to fall till the pulse became imperceptible. Giving extra glucose-saline would often cause venous engorgement without reviving the heart. A small percentage of such cases had a little rise of temperature just before death. An inspection of their bed clothes sometimes showed the presence of little blood and mucus, in the diarrhoeic stools. Were these cases of dysentery? In view of the fact that no signs or symptoms of dysentery were previously noted I am inclined to believe that it was a fresh attack of dysentery contracted from other patients through the agency, and the careless habits, of the untrained civilian staff in spite of most careful vigilance. And this attack was usually the last straw.

Another cause of death among cases with diarrhoea was the onset of cerebral thrombosis. It occurred in about 5 per cent of the series.

In cases without diarrhoea, a couple of hours before death, the main symptom complained of was a feeling of extreme debility and exhaustion. Even though the pulse was perceptible the tension was always low. Listlessness and prostration of the patient were most pathetic. He gradually went into coma before death. Injections of camphor in ether or administration of intravenous glucose made no material difference to the outcome.

During the first week of starting the hospital, a young girl in her early twenties was admitted with œdema of the lower extremities. She had walked up to the hospital. On the third morning of her stay she walked to the outside of the ward and sat in the sun, her œdema apparently having slightly improved. Half an hour later she walked back to her bed, but now she was in a state of collapse. Ten minutes later she was dead. Was she a case of beriberi? After this incident, a complete rest was enjoined on all patients, but similar cases continued to occur nevertheless.

An onset of uræmic coma was uncommon even among nephritic cases. No case of evident cerebral hæmorrhage was seen. Some of the patients who died of cerebral thrombosis or gradual heart failure may have belonged to this group, but a typical case of chronic nephritis with high blood pressure ending in heart failure was not met with. A fair number of deaths were accounted for by a terminal attack of broncho-pneumonia.

#### SCABIES

In ordinary circumstances, one has got to consider each patient individually. Is he suffering from dermatitis herpetiformis or lichen planus as there is so much itching complained of? There is no such difficulty in famine times in Bengal. In this area 80 per cent of the very

poor population are suffering from skin troubles; 95 per cent of these are cases of scabies, the remainder of impetigo, eczema, or dhobi's itch. Patients suffering from malaria are usually disappointed if they cannot get quinine, but cases of scabies are actually quarrelsome if they are denied an adequate amount of sulphur ointment.

Why is scabies so common? It is now an established fact that the infestation with *Acarus scabiei* occurs mainly through close personal contact. In this connection let me recall the famous experiment in which 25 healthy volunteers were made to sleep under blankets recently used by persons infected with scabies. No infection occurred. Then 32 volunteers were made to wear infected underclothing, only two got infected. Then volunteers were made to sleep with scabies cases, all with pyjamas on, 3 out of 4 got the infection. This is rather a startling fact which will probably make us revise our opinion with regard to the routine followed in military hospitals of disinfecting all personal and hospital clothing used by scabies patients.

The famine has hit the poor rather badly. Lack of clothing means more and more people sleeping huddled together under one blanket exactly reproducing the conditions in the experiment quoted above. The result is obvious.

But this perhaps is not the whole explanation for such a wide spread of scabies. Half of the superior nursing staff and the medical officers (including myself) also got infected. No doubt we were all in close contact with the patients but hardly ever in such intimate and prolonged contact as to get infected in such a high percentage. And there was no question of inadequate provision of clothing. I am inclined to believe that the condition of the skin has something to do with it. Let me explain.

Water in Madaripur is extremely hard, and it is immaterial whether you draw it from the river or the tube-well. Each time soap is used, a thick scum rises to the water surface. You wipe your hands on a towel afterwards, there is a yellow stain left on the cloth. This necessarily means a dry skin.

Now, the worst cases of scabies have almost invariably a very dry skin. Dry skin is obviously what the scabies mite wants. It is much easier for the acarus to find small cracks to burrow into. This to my mind is one of the additional factors affecting the spread of itch.

Again, owing to famine conditions, pityriasis as an evidence of vitamin A deficiency has been very common. This, in ordinary parlance, means a dry skin. That again means a greater susceptibility to scabies.

A suggestion has been made that scabies and oedema have both been very common during this famine, and therefore there may be some relationship between the two diseases. Nephritis (which formed only 7 per cent of the series of hospital admissions due to oedema) finds

only one thing in common with scabies, and that is they are both liable to occur more in the cold weather rather than in the hot. Inadequacy of clothing favoured suitable conditions for both diseases.

I cannot see any relationship between scabies and oedema due to causes other than nephritis except the famine and non-availability of medical attention in the early stages of various diseases that followed it.

## INANITION CASES

### A REPORT

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### Introduction

THIS article is a report on over 300 cases treated by the military unit posted in Barisal to do famine relief work. The Bakerganj district, in which Barisal is, was said to be the granary of Bengal, and yet it was one of the worst affected areas. A hospital under canvas was set up and started functioning on 28th November, 1943, with three medical officers. Although it was not possible to reach the outskirts of the district easily, with the very poor means of transport and the numerous waterways acting as barriers, yet every effort was made to make the inaccessible areas within reach of medical aid. Admission to the hospital was from (a) the civil hospital the surplus cases of which were transferred to the military hospital, (b) the destitutes' home, to which destitutes were brought from the suburbs by the missionaries, the A.R.P. and police personnel, and the touring medical officers, and (c) the out-patient department attached to the hospital. It might therefore be said that the type of cases treated in Barisal was an indication of the conditions in the Bakerganj district. For admission the patients either came walking, or were brought in stretchers if they were too ill. The cases dealt with were mostly of the severe or moderately severe types.

### Occupation

Most of the victims of starvation belonged to the working class of people, earning about ten to fifteen rupees a month. They were chiefly (a) coolies employed in the jetty, (b) ferry boat-men, (c) fishermen, (d) farmers, (e) cooks, (f) washermen, and (g) maid-servants. Beggars formed a good proportion too.

### History

Before the famine these people had lived a fairly comfortable existence. Their diet was chiefly rice, vegetables and fish. With the onset of the famine there was in most families at least one death, the cause of death being cholera, smallpox, fever or 'swelling of the body'. An interesting feature observed was that in the same family one member might be



quite well, while another was an advanced case of malnutrition. For example—

*Case 1.*—A Muslim boy, aged 8 years, was admitted with general anasarca. The face, abdomen, scrotum and legs were all markedly swollen. His sister, aged 6 years, showed not a single symptom of starvation except a temperature of  $101^{\circ}\text{F}$ . for the first two days after admission. The boy recovered in 11 days.

#### *Examination of a typical case*

*General condition.*—The patients usually appeared very poorly built, with a pinched face, prominent cheek bones, sunken chest, scaphoid abdomen, extreme wasting of the limbs and œdema of the legs and feet. In more advanced cases, the general wasting might be masked by puffiness of the face, ascites, and œdema of the scrotum or vulva, forearm and hands. The skin was dry and scaly, and the temperature normal or sub-normal and very rarely high. The eyes revealed marked clinical evidence of anæmia. No icteric tinge of the sclera was noted. The teeth were very dirty, markedly *pan-stained*, and pyorrhœa was often present.

*Circulatory system.*—The pulse rate was either normal or less than normal and, in very advanced cases, the volume and tension were very low. The heart beats were faint in advanced cases, and a systolic murmur in all the areas was present in a few cases.

*Respiratory system.*—The chest movements were limited. In cases with marked dropsy, congestion, especially of the left base, was noted. This disappeared with improvement, but pulmonary complications often set in.

*Alimentary system.*—The appetite and craving for food were there, but the patients could never understand how impaired their digestive powers were. Quite a number of them either stole or brought food from others and thus made their conditions worse. Diarrhœa was very common among the inanition cases, often intractable in the advanced ones. There were cases with no diarrhœa, a good appetite, their only complaint being the œdema. *Ascaris* infection was present in almost all the cases.

*Nervous system.*—The higher functions of the brain were normal, except in a few cases which are dealt with later. The cranial nerves were intact. The superficial and deep reflexes were present even in the most advanced cases. There was no loss of sensation in any of the patients, and tenderness of the calf muscles was present in one only.

#### *Complications*

The complications chiefly met with were: (1) malaria (diagnosed clinically), (2) bronchopneumonia, (3) cholera, (4) scabies, (5) dysentery and (6) prolapse of the rectum.

Special complications are dealt with later.

#### *Types of cases*

The findings in our hospital tallied with the findings of the Committee of Enquiry into the Effects of Starvation (vide *Treatment and*

*Management of Starving Sick Destitutes*, prepared by the Committee of Enquiry into Effects of Starvation, Indian Research Fund Association, on 1st December, 1943, from the All-India Institute of Hygiene and Public Health, Calcutta). Four types of cases were met with:—

1. Pure and simple inanition cases with slight œdema or general anasarca.

2. Inanition cases with anasarca or œdema and an intractable diarrhœa.

3. Starvation cases with symptoms of disease masked by starvation, the symptoms manifesting themselves on improvement.

4. Acute fever and relatively little inanition. This type is not dealt with in this article.

But in all these types the feature noted, as it was observed in Calcutta, was the relative rarity of marked signs of vitamin deficiency. Thus, even in the most advanced cases of inanition, one never met with a frank case of beriberi with the typical absence of jerks, tenderness and cramps in muscles, a dilated heart with tic-tac rhythm, although the presence of the œdema might be taken as a sign of vitamin-B deficiency. Similarly signs of the deficiency of the individual vitamins A, C, D and E were never met with. Thus a frank case of xerophthalmia or scurvy was not seen. This might be accounted for by the fact that the patients suffered from a multi-vitamin deficiency in which the signs of the deficiency of the individual vitamins were masked, or that they would manifest themselves only in the sub-acute or chronic stages.

#### *Treatment*

A close hair-cut was given to all the patients, and the hair was scrubbed with a hard brush and washed with soap and water. This relieved the patients of lice infection. A good bath, clean clothes and a comfortable bed contributed to recovery, and many patients have often appreciated such attention to minor details.

*Diet.*—A simple case of type 1, in which there was just wasting and no impairment of the digestive powers, improved very rapidly on the ordinary diet of rice, fish and dhal. The œdema began to disappear in a very few days, and in the really advanced cases with swelling of the face, hands and scrotum, it took only about 10 days for the œdema to subside completely. Case 1 is an example. But it was essential that *while the patient had dropsy he would be on a salt-free diet*. The ingestion of salt hindered the disappearance of œdema, or even brought it on again.

*Case 2.*—A Hindu girl, aged 12 years, was admitted on 23rd December, 1943, with considerable œdema of the limbs, marked anæmia, and diarrhœa. She was put on an ordinary diet of rice and milk at first, and later on rice and dhal (salt free), and began to improve very rapidly. The œdema disappeared completely by 29th December, 1943.

A feature observed was that the balance between the œdematous and the



stage was very delicate. Thus it was noted that cases which had been normal for many days, or belonged to type 4, *i.e.* the type with acute fever and relatively little inanition, suddenly developed œdema for a day or two even they were perfectly well, the œdema disappearing after a day or two. To give an instance :—

*Case 3.*—An orphan, aged 7 years, was admitted on 28th November, 1943, for fever, duration 10 days. The fever subsided on 3rd December, 1943, and did not appear again. On the 17th December, however, the boy developed, for no accountable reason whatsoever, œdema which disappeared after two days, *i.e.* the 19th.

Many other cases similar to the above were met with. Apart from this, a change in the diet of the patient as for instance in case 11, or sometimes the deliberate attempts of the patients with a view to prolonging their stay in the hospital, brought on the œdema. To give an instance of the latter :—

*Case 4.*—A Hindu female, maid-servant by occupation, came in with œdema of the feet on 28th December, 1943. The œdema disappeared about the 10th January. The patient was informed on the 12th that she would be discharged the next day, *i.e.* the 13th, when the œdema appeared again. A similar thing happened on the 23rd. On the threat that her children would be discharged while she would be kept in the hospital, the œdema disappeared by the 25th. This œdema, it was later discovered, was produced by the excessive ingestion of chillies and salt.

Type 2 cases, in which œdema and diarrhœa were present together, offered the greatest problem in treatment. Sometimes as in case 2 it was best to ignore the mild diarrhœa and put the patient on salt-free rice. Rapid improvement in the diarrhœa and dropsy was noted. But more often these cases had to be fed on milk, glucose-water, fruit juice, etc., increasing the diet to rice and milk and later rice and dhal on improvement. In spite of everything, advanced cases of anasæra with intractable diarrhœa were very difficult to cure. This type was commonest among the older people and invariably fatal.

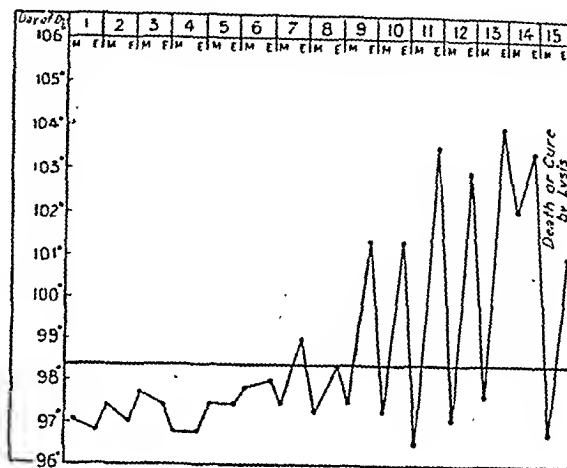
To quote an example :—

*Case 5.*—A Muslim beggar woman, aged 40 years, was admitted on 19th December, 1943, with œdema and swelling of the hands, anæmia, nutritional diarrhœa, a sub-normal temperature, and pulse rate of 60 with low volume and tension. Intravenous peptone-glucose of 200 c.cm. was given on 20th December, 1943, and again 150 c.cm. on 21st December. By the 22nd the swelling of hands had subsided and that of the feet less than before. But the diarrhœa resisted all treatment and although the œdema had lessened considerably, the diarrhœa eventually killed the patient on the 29th.

In type 3 cases in which the inanition was complicated with fever or dysentery, the fever did not usually come on till the œdema subsided, or else till there was an improvement in the patient's condition. The reason for this was that the patient was in such a rundown condition that his body had lost even the power to put up a fight against infection. With improvement, however, the body was able to combat the infection, as was evident by the rise in the temperature. To give an example :—

*Case 6.*—A Muslim girl, aged 6 years, was admitted on 28th November, 1943. The patient had œdema of the feet and no temperature. With improvement in the patient's condition the temperature shot up and the child had an intermittent fever, with the maximum temperature of 102 to 103°F. daily. Quinine was administered and the fever subsided on the 13th. The patient was discharged cured on 16th December, 1943.

The temperature chart of this type usually appeared thus :—



The fever was the one that had to be watched for most carefully, as it killed many of the patients. This type of cases was, unlike type 2, usually met with among the children especially between the ages 1 and 5. The fever and dysentery were treated along the usual lines, always bearing in mind of course that the patients were in a very debilitated condition, and therefore the dosage of drugs should be less than the usual dosage.

#### Peptone-glucose

Peptone-glucose prepared by the All-India Institute of Hygiene and Public Health was tried. For the composition, method of preparation and a detailed report on its action, a reference is invited to the article by Krishnan, Narayanan and Saukaran in the April 1944 issue of the *Indian Medical Gazette*. Its effect, as found from use in our hospital, can be summarized thus :—

(a) In an uncomplicated case of inanition with marked swelling of the body and œdema its action was in no way quicker than a salt-free diet of rice and dhal. For instance a comparison can be made between case 1 and the following case :—

*Case 7.*—A Muslim boy, aged 7 years, was admitted on 20th December, 1943. His face, hands, abdomen, scrotum, penis and legs were markedly swollen. Patient's brother and sister were both well (*cf.* case 1). He was given intravenous peptone-glucose 200 c.cm. and 100 c.cm. on the 20th and 23rd respectively. Swelling of the scrotum started subsiding by the 25th and had subsided completely by the 29th. The œdema had subsided by the 30th.

(b) In inanition cases complicated by an intractable diarrhœa peptone-glucose helped to reduce the œdema, but yet offered no cure, as the diarrhœa invariably proved fatal (case 5).

The administration of peptone-glucose was by the intravenous route. Great care had to be taken as regards the sterility and quality of the peptone-glucose; this should be port-wine in colour, with a pleasant odour. A noise should be heard on opening the bottle, the sound of air entering the vacuumatized bottle. The urine, it was said, must be examined, as the anasarca was sometimes due to nephritis. No albumin was present in any of the specimens of urine tested.

Three cases were met in the hospital (one ending fatally) showing a reaction to peptone-glucose. The bottles used in two of the cases were from the same consignment. Two other bottles were discarded as they had developed a foul odour.

*Case 8.*—A Hindu girl, aged about 9 years, was showing a very rapid improvement from a general swelling of face, abdomen, legs and feet on a salt-free diet. The peptone-glucose was administered to see if the oedema disappeared any quicker. When nearly 200 c.cm. of the preparation was given by the intravenous route, the patient started complaining of acute pain in the abdomen and began to vomit partly-digested food material. (The injection was given about half an hour after food.) The girl became blue and cyanosed, and began to pass pure blood in the stools. The pain in the abdomen did not subside. The cyanosis and passage of pure blood in the stools persisted, and the patient died two days later.

The other case was similar to the one dealt with above. The injection was from the same consignment and given after food. Here again, the patient began to vomit and complained of acute pain in the abdomen. Fortunately only 50 c.cm. had been administered before these untoward symptoms appeared. The injection was stopped, and the patient recovered after some time. The third case had rigors after the peptone-glucose injection.

### Diet

The diet prescribed by the Committee of Enquiry into the Effects of Starvation was followed—fluid, milk and gruel diets. But the gruel had to be discontinued as the patients did not relish it and said that it was very insipid and worsened their condition. The number of desertions began to increase, and therefore rice, vegetables and dhal had each to be cooked and served separately. Butter milk or *ghol* was a very palatable form of giving milk, and had the additional value of containing more of vitamin B. It was appreciated by all patients. Moreover it was very easily prepared.

To combat the vitamin deficiencies, multi-vit tablets, vitamin B tablets, A and D capsules, shark liver oil were given to all the patients. Oranges were given especially to children and marked cases of inanition.

Scabies, cholera, broncho-pneumonia, prolapse of the rectum were treated along the usual lines.

### Mortality

Mortality was highest between the ages 1 and 5, and above 30. Children between 6 and 10 had

the best chances of recovery. The commonest cause of death in the children was fever. In the older people nutritional diarrhoea was responsible for death.

### Special features and complications

A few cases in which special features were noted may be mentioned.

(a) *Mental symptoms.*—Three cases among children and three in adults were very illustrative, especially the former.

*Case 9.*—A Muslim boy, aged 7 years, was admitted with oedema on 28th November, 1943. The patient was very emaciated, skin dry and scaly and oedema slight. No temperature. This boy ran away on the 3rd and was brought back on 8th December, 1943. He had meanwhile also developed a dysentery. It was then noted that the patient exhibited mental symptoms, talking and laughing to himself. A very characteristic feature observed in this boy was the extreme look of anxiety always present on his face, even though he had improved considerably and special care was paid to him. This patient later developed broncho-pneumonia, which was cured, but suddenly took a bad turn and died.

*Case 10.*—A Muslim boy, aged 9 years, was a very interesting case. He was brought walking into the hospital on 31st December, 1943, with oedema of legs and feet, puffiness of face and lids and a temperature. Patient was a very intelligent child and answered questions accurately. By the 8th January the swelling and fever had subsided and about 10th January, 1944, the patient began to exhibit mental symptoms. He used to walk round the wards, discarded all his clothes and kept on muttering to himself. The appetite was normal, and diarrhoea rare. The boy began to get worse, sang and laughed and talked to himself both during day and night—all his thoughts being based only on food. In spite of all this the patient was conscious of his surroundings and of what was going on around him, and sometimes caught an occasional phrase and used it as a song. On the 15th January, the boy had an epileptiform type of fit in which the reflexes were lost, heart beats irregular and respiration prolonged and deep. Morphia and whiffs of chloroform had to be administered. The boy gradually began to get worse, lost the powers of extending his legs and thighs, the muscles of which were wasted. Bed-sores developed about the 20th January. By then the patient kept his legs and thighs always flexed and could not straighten them.

Intravenous peptone-glucose, intramuscular quinine, cholera vaccine 1 c.cm. (intended to be a protein shock) had no effect. A lumbar puncture was done on 4th March, and the spinal fluid was found to be under pressure, clear; the globulin test was negative. During all this period, 20th January to the beginning of March, the patient was given constant massage, and the legs were stretched. The reflexes and sensation in the wasted limbs were still intact.

Signs of improvement were noticed about the 25th February, the first of which was that the patient slept better during the nights. By 7th March the bed-sores started healing, and by the 21st April, 1944, the boy had gained much weight, was able to walk about, and his mental condition was normal.

(b) Another special complication noted was the wasting of the leg and thigh muscles and the eventual ankylosis or fibrosis of the knee joint, with the thighs and legs always kept flexed. This was noticed in the case mentioned above and also in another case.

*Case 11.*—A Hindu girl, aged 13 years, was admitted with marked general anasarca. The appetite and the digestive powers were normal, and with nourishment the dropsy subsided. The muscles began to waste

and eventually the legs and thighs were kept flexed, and the knee joint ankylosed. The reflexes and sensation were intact. Massage and stretching were carried on without any improvement being noticed.

It was decided to transfer this patient to the destitutes' home, as the patient was eager to go there, and it was thought that a change might do her good. Instead the girl developed diarrhoea and oedema as the gruel diet given in the destitutes' home did not agree with her. This happened on two occasions, and the oedema and diarrhoea subsided and the patient became well as soon as she was brought back to the military hospital. This girl, the writer was informed, eventually died in the civil hospital.

(c) Convulsions in children or epileptiform types of fits were noted in four cases. These usually occurred before death.

### Summary

(1) A report on the inanition cases met with in Barisal in the Bakerganj district is given.

(2) Symptoms, types of cases and treatment are discussed.

(3) Special features and complications are dealt with.

### Acknowledgments

My thanks are due to Lieut.-Colonel H. B. MacEvoy, I.M.S., and other senior officers.

## EFFORT SYNDROME

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HURST (1943) defines 'effort syndrome' as a condition in which the symptoms and signs produced in healthy people by excessive exercise are called forth by an effort which should normally give rise to no unpleasant symptoms and in which no physical signs of organic disease are present. During the last war it was variously known as 'soldier's heart', 'disordered action of the heart' and 'irritable heart of soldiers'. Though not uncommon among civilians, their relative frequency among soldiers led to the use of the term 'soldier's heart' for describing functional cardiac disorders. The Americans (1941) call it 'neuro-circulatory asthenia' a long, though descriptive, term. The term 'effort syndrome' introduced by Lewis (1919) to replace the undesirable diagnosis such as 'disordered action of the heart' is itself not a happy expression, as it lays undue stress on the relation of the syndrome to effort. As the condition is undoubtedly a neurosis, the term 'cardiasthenia' will be more apt and descriptive.

In the 1914-18 war, from the beginning up to 31st May, 1916, 2,503 men were discharged from the British army on account of 'heart disease'. The problem of invaliding on account of soldier's heart became so serious that the war

office arranged for the investigation and treatment of all heart cases at the Hampstead Hospital under Sir Thomas Lewis. At the same time five heart centres were established in France. The experiment of establishing special centres was eminently successful in that 50 per cent of cases of 'disordered action of the heart' were detained for duty in France. Lewis' investigations established the fact that there was no organic heart disease in 'disordered action of the heart'. In the present war the number of cases has remained limited. Only three special centres, two in England and one in Scotland, have been established. The total admissions into the largest of these was only about 700 up to May 1941 (Wood). I have no statistics regarding the total number of cases of 'effort syndrome' reported in the Indian army so far. Hence I am unable to give any idea as to its incidence. Out of a total of 4,286 medical cases (excluding 6,277 cases of malaria), 59 (1.3 per cent) were diagnosed as 'effort syndrome'. The proportion becomes 0.59 per cent when calculated from the total admissions to a medical division.

**Ætiology.**—In the army the highest incidence is of course in young adults. In civil life the highest incidence is at a later age than in the army. Craig and White (1934) found the average to be 35 years. In the 59 cases studied, only four were above the age of 30, the remaining 35 varying between 19 and 30.

Current literature on the subject mentions several factors contributing to the causation of 'effort syndrome.' Hurst in his book on medical diseases of war enumerates the following factors:—

(1) Feeble circulation due to either congenital cardiac insufficiency or feeble development resulting from sedentary occupation or old heart strain.

(2) Intoxication as toxæmia from infections, excessive smoking, alcohol, cordite poisoning, or gas poisoning.

(3) Over exertion.

(4) Nervous factor involving some aberrant psychological make-up of the individual.

A man with a narrow ill-formed chest and small heart has a circulation sufficient for routine work, but is unable to cope with increased strain as he has no sufficient reserve power. In civil life, therefore, his habits are sedentary. He is, however, liable to break down during the training periods of his army life.

The same will be the case with one who, in spite of the absence of physical defects, has pursued a sedentary occupation in civil life. Lewis found that 57 per cent of 543 patients suffering from 'effort syndrome' were recruited from sedentary or light occupations. It is the sudden change from sedentary to strenuous life, which preliminary military training involves, that causes the break-down. Perhaps a slower process of initiation which is

possible only in the absence of emergencies would prevent the break-down in this type of individuals.

There are again those who are accustomed to severe physical exertion during civil life, but who have occasionally 'strained' their hearts by taking unwonted exercise on previous occasions. They are liable to succumb under the stress and strain of army life.

Twenty-one cases in this small series were post-infective, 12 were post-malaria, 5 post-dysenteric, 3 post-pneumonic and one after infective hepatitis. Trench fever was probably the most common infection to be followed by 'effort syndrome' in the last war. Epidemic catarrhal jaundice was a common cause of 'effort syndrome' in the Gallipoli campaign.

Whatever may be the type of individual concerned, be he the one with a congenitally weak circulation, or one with sedentary habits or one with lowered vitality after infection, it is a sudden over-exertion, far beyond the limits of his reserve power that precipitates an attack of 'effort syndrome'. The strain on the heart resulting from the unwonted physical effort, produces a train of cardiac symptoms which tend to persist even after the cause is removed. The persistence of cardiac symptoms in the absence of any organic heart lesion can be attributed only to a physiological factor, which is evidently brought about by the worry, anxiety and nervous tension which are unavoidable in active military service. Walshe points out how difficult it would be for the most normal man to escape intact with his mind untarnished from an inquisition of this fantastic order. Degraff classifies it with neurasthenia, that group of borderline disorders wherein fatigue is prominent and the other symptoms present are referred to almost any system or organ. It is nothing more than a manifestation of an anxiety neurosis. Otherwise it is impossible to explain how symptoms of cardiac disease can persist without any organic disorder of the heart even after the overstrain has ceased to exist.

Attempts have been made to find a physiochemical basis for the symptoms of effort intolerance. During the last war, not very successful attempts were made by Haldane *et al.* (1919), Drury (1920), Briggs (1920) and also several others. Recently Soley and Shock (1938) have put forward the idea that respiratory alkalosis following hyperventilation is responsible for some of the symptoms of 'effort syndrome'. This view has not been confirmed by Guttman and Jones (1940).

Jones and Scarisbrick (1943) have shown that blood lactic acid level did not rise to the same height as in normal individuals when they were all exercised to the level of exhaustion. Respiratory alkalosis did not occur. The most obvious conclusion to be drawn is that the poor effort response in patients with 'effort syndrome' is due to lack of persistence. Their work confirms the view that there is a

psychological rather than a physiological anomaly underlying 'effort syndrome'.

The war office classification (41) of 'effort syndrome' is elaborate and satisfying. The cases are divided into four groups with two subdivisions in each of the first two:—

*Group I.*—(1) With gross physical defects.

(2) With gross physiological manifestations.

*Group II.*—Chronic and long-standing cases in whom the attention of the subject has been drawn to his heart before admission to the service.

(1) Cases who have been unable to maintain heavy work in civil life.

(2) Cases with better physique whose attention has been unwisely drawn to their hearts.

*Group III.*—Recent cases. Symptoms developed after service.

*Group IV.*—Post-infective.

This classification is extremely helpful in judging prognosis and planning the disposal of patients. Perhaps a simpler clinical classification would be:—

(1) Defective. (Those with gross physical or psychic defects.)

(2) Undeveloped. (Those feebly developed due to sedentary occupation.)

(3) Suggested. (Those to whom heart disease has been suggested.)

(4) Post-infective.

### Symptoms

Excessive physical exertion is the precipitating factor in almost all the cases. The majority of the cases being post-infective, the onset occurs usually on returning to duty after an illness before the patient feels completely fit. Even a normal man, if he is not under training for some time, will feel the strain when he is suddenly called upon to perform the arduous duties associated with active army life. More so will it be in the case of one who has been temporarily weakened by toxæmia of an infectious disease. As the nervous strain apart from the physical strain is greater in such an individual, he is prone to exhibit symptoms of neurosis. In many cases actual cardiac symptoms are preceded by nervous symptoms resulting from mental strain associated with toxæmia and fatigue. General symptoms such as headache, lassitude, irritability, insomnia and giddiness are common at the beginning. Tremors of the hands and excessive sweating especially of the palms and soles are not uncommon initial symptoms.

The characteristic main symptoms are essentially the same as that of organic heart disease, namely breathlessness, palpitation, precordial pain and a feeling of exhaustion. In the present series of cases, breathlessness alone was found in 10, breathlessness and palpitation in 15, and all the three symptoms of breathlessness, pain and palpitation were found in 26 cases. In eight cases, other symptoms such as

abdominal pain, a nervous type of cough, vague pains in other parts of the body coupled with one of the above main symptoms were observed.

Physical signs pertaining to the heart itself are invariably absent. The size of the heart is normal except in the first group of cases, where a small vertical heart is not an uncommon finding. Wood found no enlargement of the heart in any of the 500 cases he screened. Instability of the heart rate is invariably present. Only in a few cases, especially when the condition is partly due to excessive smoking, there is persistent tachycardia. The resting rate is normal in all other cases, but the slightest exertion or excitement unduly accelerates the pulse. Sitting up in bed or assuming the erect posture may increase the pulse rate by 30 or 40 per minute. The blood pressure is normal at rest except in the endocrine type. A systolic murmur at the apex and at the pulmonary area may be heard in some cases. Lewis found a systolic murmur in 42 per cent of 462 such patients. He thinks that 'the presence or absence of systolic murmurs is of no value in estimating the soldier's capacity for work irrespective of the character, condition, or point of maximum audibility of the murmur'.

Parkinson (1916) demonstrated that the electrocardiogram is normal in 'effort syndrome' and remains so after effort. Exercise tolerance was normal in 35 cases and slightly diminished in 24 cases.

It is worth while to bear in mind the two special points stressed by the medical directorate pamphlet, namely (a) an over active heart must not be mistaken for an enlarged heart by feeling the furthest-out site of pulsation, and (b) a slight systolic murmur must not be mistaken for organic disease.

**Diagnosis.**—The diagnosis of 'effort syndrome' is dependent on the absence of physical signs of organic heart disease while the subjective symptoms of cardiac disorder are present. Differential diagnosis has to be made from such conditions as sub-acute bacterial endocarditis, valvular disease and angina, and from incipient phthisis. A degree of pyrexia is invariably present in endocarditis; systolic and diastolic murmurs, and symptoms of infarction in various organs are found. Murmurs of valvular disease are often characteristic. Moreover a history of acute rheumatism or chorea can very often be elicited. A functional systolic murmur can easily be distinguished by its non-conduction, better audibility in the pulmonary area and its variability. Moreover there is no cardiac enlargement. Angina is rare in young men, the age period in which 'effort syndrome' is common. True angina is retrosternal while the functional angina is most often below the heart. All symptoms of 'cardiasthenia' such as palpitation, tachycardia and even precordial pain may be found in incipient tuberculosis. But the presence of the temperature disturbance in some part or other of the day, a high sedimentation

rate and a radiograph will help in the differential diagnosis.

**Prognosis.**—Type one cases with gross physical or psychological defects are not fit for the excessive physical exertion which army life involves, and hence they should be never recruited at all. If they are recognized after they have somehow trickled into the army, they must be immediately boarded out. Most cases of the second type may have to be sent out of the army as unfit. A few however can either be made fit by graduated training, or can be employed in a lower category. The majority in the third group and almost all in the fourth can be made fit for duty. In the present series, six were invalidated, seven were 'recategorized', and 32 were returned to duty.

**Treatment.**—Prophylaxis, so far as the army is concerned, consists in the elimination of the unfit by boarding out, in the institution of slower and less rigorous training for the undeveloped, and in careful graduated training during convalescence in the post-infective period. No suggestion as to heart disorder should be made even when subjective cardiac symptoms are present after an infectious disease. The old official diagnosis of 'disordered action of the heart' or 'soldier's heart' has very wisely been abandoned. The essential part of the treatment consists in convincing the patient that he is not suffering from any heart disease whatsoever. In the vast majority of cases, hospitalization is not required. The cases should be recognized by the regimental medical officers of units. The patient's symptoms are genuine though functional. Firm but sympathetic handling is required. The medical officer must try to gain the confidence of the patient and convince him that he is not suffering from any organic disorder and that he is sure to return to normal. I do not agree that the man suffering from 'effort syndrome' should be kicked back to full duty once the diagnosis is made. Invalidism could be avoided in most of the cases belonging to groups III and IV, if they are considered as ambulatory patients in the initial stages until the medical officer is able to convince them that there is no organic sickness in them. If the medical officer is able to convince the patient the first time he sees him, he can be returned to duty the same day. Only if the medical officer finds that the patient does not improve in two weeks should he be sent to special training centres or general hospitals. Unfortunately most of the cases that get admitted in hospital should not have been there at all. Fifty cases were sent in with a wrong diagnosis. Out of the nine cases that came as 'effort syndrome', three could have been disposed off by the medical officer or lower medical formations.

The general principles adopted by the special unit of the 23 B. G. Hospital were as follows:—

'The men are kept together. They are subject to the ordinary discipline and routine.



apart from graded exercises, and are under the direction and observation of a specially selected physical instructor. On admission to the hospital, they are carefully examined once. They are not kept in bed. Subsequently there are no routine examinations, the observation of the physical training instructor and general observation of the men after exercise being found to be sufficient. It is frequently unnecessary to examine men on discharge when their progress justifies return to their units'.

Though 'effort syndrome' is a form of neurosis it should not ordinarily need the special efforts of a psychiatrist. The amount of knowledge of psychological medicine possessed by the ordinary medical man is quite adequate to cope with the situation in most cases, as the essence of treatment consists in convincing the patient that he is not a patient at all. Some mishandled long-standing cases however do require the skilled labours of the psychiatrist.

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### SULPHADIAZINE IN THE TREATMENT OF BUBONIC PLAGUE

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THE value of some of the sulphanilamide derivatives in the treatment of plague has now been well recognized. In a field trial conducted at Bettiah, Bihar, in 1940, it was found that both sulphathiazole and sulphapyridine reduced the case mortality in bubonic plague to a significant extent. These results were confirmed in subsequent trials carried out at Latur in 1940 and 1941. Sulphadiazine, another heterocyclic derivative of sulphanilamide, which has been found to be equal or superior to sulphathiazole or sulphapyridine therapeutically in pneumococcal and meningococcal infections, has not so far been tried by us in this disease. When, therefore, plague

broke out in Poona in 1943, the opportunity was utilized to test the value of this drug in this disease. For comparative purposes sulphathiazole, previously found to be the drug of choice because of its low toxicity and good therapeutic efficiency, was also given in alternate cases. We are indebted to Dr. Cushing of the National Research Council of America for adequate supplies of the drug for this trial.

#### Material and methods

The trial was conducted in the Infectious Diseases Hospital at Poona, and lasted from middle of November 1943 to middle of February 1944. During this period, 185 cases were admitted for treatment, of which 182 turned out to be cases of plague.

The two treatments were given in strict rotation, no selection of cases being made. Thus the first patient received sulphathiazole, the second sulphadiazine, the third sulphathiazole, the fourth sulphadiazine, and so on. In every patient, on admission, the diagnosis was first made on clinical grounds, and before any treatment was given. 0.5 c.cm. of blood was drawn from a vein and spread in equal quantities on two agar slopes. This was done to detect the presence or absence of plague septicæmia at the time of admission, and its degree if present. Immediately after withdrawal of blood, the treatment was commenced. The cultures were seen after incubating the slopes for two days at room (27°C.) temperature. In non-septicæmic cases in whom the clinical diagnosis was certain, no further bacteriological confirmation was sought for, but every non-septicæmic case which presented an atypical picture was bacteriologically confirmed by making a bubo puncture and by culture of the aspirated material. Puncture of the bubo in every non-septicæmic case was avoided as a routine, as previous experience had shown that bubo puncture in some cases led to a worsening of the patient's condition.

#### Dosage and administration

*Sulphadiazine*.—An initial dose of 4 gm. was followed by 2 gm. four hours later. One gm. was then given every four hours. In this way the patient received 10 gm. of the drug on first day, and 6 gm. on subsequent days. As the trial progressed it became evident that extremely serious cases would not respond to this dosage. Some very serious cases, therefore, received 6 gm. as the initial dose, 2 gm. four hours later and 1 to 1.5 gm. every four hours subsequently. The patient thus received 14 gm. on first day and 6 to 9 gm. on subsequent days.

*Sulphathiazole*.—The first 46 sulphathiazole cases received an initial dose of 2 gm., 2 gm. four hours later and 1.5 gm. every four hours till the end of first 24 hours. One gm. was then continued four hourly on subsequent days. These cases thereby received 10 gm. on first day and 6 gm. a day subsequently. As very serious or moribund cases did not respond to this dosage, and the severity of the cases also seemed to be on the increase as the epidemic progressed, subsequent cases received 4 to 6 gm. as the initial dose, 2 gm. four hours later, and 1 to 1.5 gm. every four hours subsequently. This group thus received 12 to 14 gm. on the first day and 6 to 9 gm. on subsequent days.



In cases treated with sulphadiazine, half the initial dose was given intravenously and the rest orally. Subsequent doses were given orally unless the patient was comatose or unable to swallow for any reason. In cases treated with sulphathiazole, the first 46 cases received their initial and subsequent doses orally unless there were reasons to give it parenterally. Later cases received part of the initial dose, i.e. 2 gm. intravenously and the rest of the dose orally. Subsequent doses were given orally unless otherwise indicated. We could not give more than 2 gm. of sulphathiazole intravenously, as higher doses were not tolerated well by the patient. For intravenous injections a 5 per cent solution of sodium salt of the two drugs was used. Both the drugs were continued until the patient was afebrile for at least 48-hours with distinct improvement in general condition. In any case, the drugs were not given for more than 12 days.

### Blood concentration

The level of drug concentration in the blood was estimated at a fixed time once daily in the morning. It was desired to obtain a blood concentration of 5 to

concentration of 5 to 10 mg. per 100 ml. and the remaining a concentration lower than 5 mg. per 100 ml. In spite of using a higher dosage, therefore, we did not succeed in getting a higher blood concentration in a large number of cases in the second group.

In cases treated with sulphadiazine, the concentration attained was higher and more uniform than that in sulphathiazole cases. In the group that received 10 gm. on the first day and 6 gm. daily subsequently, 75.7 per cent of the cases attained a concentration of over 10 mg. per 100 ml., while in the second group which received 14 gm. on first day and 6 to 9 gm. on subsequent days, 86.6 per cent attained the concentration of between 15 and 20 mg. per 100 ml. In these cases, therefore, a higher concentration was more easily attained with the increase in dosage than in sulphathiazole cases. These results are recorded in table I.

### Results

Of the 182 cases of plague treated in the hospital, 2 cases left while still very ill, leaving 180 cases for consideration. If these cases are

TABLE I  
*Relation of dosage to concentration in blood*

Drug	Amount of drug given on 1st day	Total number of cases	NUMBER OF CASES ATTAINING THE VARIOUS CONCENTRATIONS				
			Concentration in mg. per 100 ml.				
			1-5	5-8	8-10	10-15	15-20 and over
Sulphathiazole ..	10 gm.	38	14 36.8%	21 55.2%	3 7.8%	0	0
	12-14 gm.	36	9 25.0%	14 38.8%	11 30.5%	2 5.5%	..
Sulphadiazine ..	10 gm.	66	0	10 15.1%	6 9.0%	37 56.0%	13 19.6%
	14 gm.	15	0	0	0	2 13.3%	13 86.6%

TABLE II  
*Results in all plague cases and in cases with plague septicaemia at the commencement of treatment*

Treatment	ALL CASES			SEPTICÆMIC CASES		
	Cases	Deaths	Mortality, per cent	Cases	Deaths	Mortality, per cent
Sulphathiazole .. ..	89	30	33.7	53	28	52.8
Sulphadiazine .. ..	91	20	21.9	53	19	35.8
Iodine (intravenously) ..	165	96	58.1	91	84	92.3

10 mg. per 100 ml. of free sulphathiazole and of 10 to 15 mg. per 100 ml. of free sulphadiazine. In the first group of cases which received 10 gm. of sulphathiazole on the first day and 6 gm. on subsequent days, 63 per cent of the cases attained the desired concentration of 5 to 10 mg. per 100 ml., while the remaining cases attained a concentration between 1 and 5 mg. per 100 ml. In the second group which received a higher dosage of 12 to 14 gm. on the first day and 6 to 9 gm. a day later, 5.5 per cent of the cases attained a concentration of 10 to 15 mg. per 100 ml., 69.4 per cent attained a

considered irrespective of the dosage used, the results shown in table II were obtained with the two treatments. For comparative purposes, combined figures of results obtained in cases treated with iodine in three previous trials (1940-41) are included in the table.

Table II incorporates on the left side the results of treatment in all the 180 cases without making any differentiation into septicæmic or

non-septicæmic cases, and on the right side the results of treatment of cases which had septi-cæmia at the commencement of treatment. During the field trials it has been noticed that the most important factor which decides the issue in human plague is the development and degree of septicæmia. If the lymph glands prevent the spread of infection to the blood stream, and the infection remains localized, spontaneous recovery results in many cases. On the other hand, if the organisms pass the lymph gland barrier and invade the blood stream, death almost invariably follows unless an effective curative agent is given to control the infection. Thus a truer picture of the results of any treatment is obtained if only those cases are considered which have septicæmia at the time the treatment is started.

The results shown in table II include every patient that died. For a correct appreciation of the value of the drug, however, it is necessary that cases moribund at the time of admission and dying within 24 hours be excluded from account as we found that sulphonamides were not effective within such a short time in human plague infection. In the sulphathiazole group there were 14 moribund cases, and in the sulphadiazine group there were 10. The results obtained after excluding these 24 moribund cases are given in table III. In table IV these results are analysed according to the different dosage used.

No difference is seen between the therapeutic effect of higher and lower doses of sulphadia-

zine. In sulphathiazole cases, the results of the higher doses appear to be inferior to those of the smaller ones ; but it must be remembered that actually the higher dosage of sulphathiazole used in 36 cases raised the concentration of the drug in blood over 10 mg. per cent in only 2 (or 5.5 per cent) cases, although a slightly higher percentage of cases, i.e. 69.4 per cent, attained a concentration of 5 to 10 mg. per 100 ml. In both the groups, therefore, the concentration obtained in the blood was about the same. The slightly higher mortality in this group thus appears to be due to a greater severity of infection rather than to a comparative ineffectiveness of the higher dosage. Of the thirteen patients that died in this group, four had secondary plague pneumonia on admission, and five others showed evidence of cardiac failure or severe toxic symptoms such as coma, restlessness, picking at bed clothes or terminal diarrhoea.

Toxic reactions

In order to reduce the toxic reactions of the drugs, the patients were encouraged to drink plenty of water, and care was taken to see that the patients maintained a urinary output of at least 1,200 to 1,500 c.cm. a day. Alkalis were also given as a routine to every patient to reduce the acidity of urine. No serious toxic reactions were encountered in any of the cases in this investigation, though 15 cases treated with sulphathiazole and 6 cases treated with sulphadiazine developed toxic reactions of a

TABLE III  
Results after the exclusion of moribund cases

Treatment	ALL CASES			SEPTICÆMIC CASES		
	Cases	Deaths	Mortality, per cent	Cases	Deaths	Mortality, per cent
Sulphathiazole .. ..	75	16	21.3	40	15	37.5
Sulphadiazine .. ..	81	10	12.3	43	9	20.9
Iodine (intravenously) ..	149	80	53.6	75	68	91.0

TABLE IV  
Results in relation to different dosage

Treatment	Quantity of drug given on 1st day	ALL CASES			SEPTICÆMIC CASES		
		Cases	Deaths	Mortality, per cent	Cases	Deaths	Mortality, per cent
Sulphathiazole ..	10 gm.	39	3	7.69	19	3	15.78
	12-14 gm.	36	13	36.11	21	12	57.14
Sulphadiazine ..	10 gm.	66	8	12.12	34	7	20.58
	14 gm.	15	2	13.33	9	2	22.22

mild nature. Table V gives the number and incidence of these reactions:—

phonamides. Iodine was the drug then most widely used in different hospitals in India and

TABLE V  
*Toxic reactions*

Toxic reactions	SULPHATHIAZOLE		SULPHADIAZINE	
	Number of cases	Incidence, per cent	Number of cases	Incidence, per cent
Nausea and vomiting ..	2	2.6	<i>nil</i>	<i>nil</i>
Spasmodic abdominal pain ..	5	6.6	2	2.4
Pain in muscles and joints ..	2	2.6	2	2.4
Dermatitis ..	4	5.3	<i>nil</i>	<i>nil</i>
Leucopænia (below 3,500) ..	<i>nil</i>	<i>nil</i>	2	2.4
Drug fever ..	1	1.3	<i>nil</i>	<i>nil</i>
Oliguria ..	1	1.3	<i>nil</i>	<i>nil</i>
TOTAL ..	15	20.0	6	7.3

Even as regards these mild reactions recorded in the table, it will be seen that the incidence is low, but the incidence in cases treated with sulphathiazole is approximately three times as frequent as that in the sulphadiazine-treated cases. In an infection like plague it is difficult to determine if a particular toxic symptom that is present has developed as a result of the disease or of the drug, as many of the reactions that arise owing to the toxicity of the drug can also arise as a complication of the disease. It is for this reason that we have included in the above table only those cases in whom the toxic reactions looked to have arisen beyond doubt as a consequence of the drug therapy. It is possible that the incidence of some of these reactions such as nausea, vomiting, drug fever, etc., is more frequent than that given in the table, but we have excluded all those cases where we could not determine the cause with any degree of certainty.

#### *Comment*

Table II shows results obtained in all cases of plague taken together without differentiation into septicæmic and non-septicæmic, and also separately results in septicæmic cases alone. This includes all patients that died, irrespective of whether they died within 3, 12, 24, or more hours of admission. Of the 89 patients treated with sulphathiazole, 30 died giving a mortality of 33.7 per cent and of 91 patients treated with sulphadiazine, 20 died with a mortality of 21.9 per cent. In severe cases, *i.e.* cases with septicæmia at the commencement of treatment, in 53 cases treated with each drug a mortality of 52.8 per cent occurred in sulphathiazole cases, and 35.8 per cent in sulphadiazine cases. A better idea of curative value of these drugs would be obtained if we compare these results with those obtained in plague cases with other treatments that were in vogue before the discovery of sul-

it would give a better idea if we compare the present results with those obtained in cases treated with iodine. In 165 cases treated with iodine during the course of three field trials (1940-41), a mortality of 58.1 per cent was obtained in all plague cases together. Ninety-one of these were septicæmic, and in them 84 died giving a mortality of 92.3 per cent. But even iodine possesses a certain curative value, and if these cases had been treated only symptomatically the mortality would have been still higher. If we compare this mortality with that obtained in cases treated with the two sulphonamides it will be seen that both the drugs have produced a significant reduction in the case mortality, the percentage of deaths being 33 and 21 in all cases, and 52 and 35 in septicæmic cases respectively.

But these results do not convey a correct idea of the value of the drug. They include cases which were moribund at the time of admission and in whom, therefore, an extensive destruction of the tissues of the vital organs had resulted before the treatment was commenced. No drug, however effective, can be expected to produce cure under these conditions, and for a correct appraisal of the value of these drugs, therefore, it is necessary to exclude all such cases in whom irreparable damage had occurred before the treatment was commenced. Table III records results obtained after the exclusion of such moribund cases. Here sulphathiazole cases show a mortality of 21 per cent in all cases and 37 per cent in septicæmic cases, while sulphadiazine cases a mortality of 12 per cent in all cases and 20 per cent in septicæmic cases. (In cases treated with iodine in previous trials the mortality after excluding moribund cases was 53.6 per cent in all cases, and 91.0 per cent in septicæmic cases). Both these drugs thus show a very significant reduction in the case mortality.

If the results of the two drugs are compared, those of sulphadiazine appear to be slightly superior to those of sulphathiazole, but statistically the difference is not significant. The effect of the two drugs on the course of temperature appears to be the same. In plague, unlike pneumococcal pneumonia, the temperature falls by lysis, and in many cases it is very irregular. Consequently, it is difficult in many cases to determine the exact hour at which the temperature has fallen to normal. If, however, we consider only those cases which showed a regular fall of temperature, in cases with no septicaemia the temperature came down to normal on an average in 80 hours, and in cases with septicaemia on an average in 113 hours in the case of both the drugs. It was, however, noticed that given the same doses, sulphadiazine maintained a higher blood concentration than sulphathiazole, and that the level of blood concentration, high or low, could be more easily maintained with sulphadiazine than with sulphathiazole.

The number of cases treated did not permit of an optimal dose being accurately worked out, but 10.0 gm. on first day and 6.0 gm. a day on subsequent days in the case of both drugs gave good results.

#### Summary

1. A report of treatment of 180 cases of plague with sulphadiazine and sulphathiazole in an epidemic at Poona is given.
2. The case mortality was 12 per cent with sulphadiazine therapy and 21 per cent with sulphathiazole therapy in all cases treated exclusive of those moribund at the time of admission and died within 24 hours. These results as compared to the case mortality of 53 per cent in cases treated with iodine, the usual hospital treatment in vogue in some previous trials, show a significant reduction in mortality.
3. Even in cases which were septicaemic at the commencement of treatment, sulphadiazine and sulphathiazole have reduced the case mortality to 20 and 37 per cent respectively as against 91 per cent in iodine treated cases.
4. The results of sulphadiazine treatment appear to be slightly better than those of sulphathiazole treatment but the difference is not statistically significant.
5. With the same dosage, sulphadiazine maintained a higher blood concentration than sulphathiazole.
6. No serious toxic reactions were encountered in cases treated with either of the two drugs. Even the incidence of mild reactions was low. However, sulphadiazine on the whole produced fewer toxic reactions.

My thanks are due to the Director, Haffkine Institute, Bombay, for his keen interest and active help in this investigation, and to the Director of Public Health for the Government of Bombay, Poona, for giving all facilities to conduct the trial.

## ON THE POSSIBILITY OF USING OIL OF TURPENTINE FOR THE TREATMENT OF SCABIES

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and

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WHEN it was noticed that the incidence of scabies is at present extremely high and that drugs such as benzyl benzoate, mitigal, tetmos, etc., are not available in this country, it was felt that it would be worth while to undertake an investigation with the object of discovering a sarcopticidal drug which would not only be efficient but would also be readily available.

In this connection, a large number of indigenous preparations commonly used for scabies in this country were tested, and in course of this investigation oil of turpentine was observed to possess properties whereby the mite was quickly overwhelmed and was soon killed on contact outside the body. The oil was used in the form of an emulsion and was prepared as follows:—

Oil turpentine, B.P.	20 parts	Soften the soap with
Soap shavings (bar soap)	.. q.s.	water; mix the
70 per cent alcohol	80 parts	oil and the soap
(If necessary the common methylated spirit may be used after dilution).		thoroughly in a
		pestle and mortar; mix the spirit gradually.

N.B.—90 per cent alcohol makes a very good emulsion, but for economy 70 per cent may also be used. The emulsion must always be well shaken before use.

Benzyl benzoate was first introduced by Kissmeyer (1937) in the treatment of scabies.\* Since then it has been tried extensively and has been recognized to be the most powerful sarcopticidal drug so far discovered. It is also the most useful drug from the point of view of treatment. In a comparative study on the action of benzyl benzoate and oil of turpentine on mites, the results shown in table I were obtained.

The observations were carried out under the dissecting microscope by placing the mite on the dorsum of the hand, and a minute drop of the fluid was then allowed to run down the skin. As soon as the skin was dry, the mite was transferred to a glass slide. The movement of the legs was taken as an indication that it was still living.

It had been previously observed that mites, when treated with either resin-alcohol or gum arabic mixture on a glass slide, were 'killed' within 10 to 15 minutes, but when the experiments were repeated on the hand, they appeared

\*It is believed that it was used for this purpose many years before this, but that its use had been abandoned.—Editor, I.M.G.

TABLE I

Effects of oil of turpentine and benzyl benzoate emulsions on adult female *Sarcoptes scabiei* var. *hominis*

OIL OF TURPENTINE							BENZYL BENZOATE, 20 PER CENT WITH AN EQUAL QUANTITY OF ALCOHOL AND SOFT SOAP							REMARKS
Strength of alcohol used	Number of mites used for each experi- ment	Total number of mites experimented upon	Maximum death time (on hand)		Average death time (on hand)		Strength of alcohol used	Number of mites used for each experi- ment	Total number of mites experimented upon	Maximum death time (on hand)		Average death time (on hand)		
Per cent			min.	sec.	min.	sec.	Per cent			min.	sec.	min.	sec.	
50	1	5	4	45	4	10	90	1	7	2	0	1	27	According to Mellanby <i>et al.</i> (1942) the mites are killed within 5 minutes of contact with benzyl benzoate away from the body.
70	1	20	2	5	1	42	..	..	..	..	..	..	..	
90	1	7	2	0	1	20	..	..	..	..	..	..	..	

dead as soon as they came in contact with the mixture but soon afterwards they were able to free themselves completely of the entanglement.

It has been claimed by Mellanby, Johnson and Bartley (1942) that benzyl benzoate, when applied to the skin without any preliminary cleansing, is able to reach the mite in the burrow. They are of the opinion that a large percentage of the mite population on the body of a person can be eliminated by this process. With turpentine we have also observed identical results; after its application on the skin, mites killed in the burrows have been extracted after 24 hours. But it must be clearly recognized that neither benzyl benzoate nor turpentine is capable of penetrating the healthy skin. When a female mite was allowed to burrow, external application of either benzyl benzoate or turpentine produced no appreciable effect on the mite within half an hour. The fluid was applied at the time when the mite had just disappeared from view. Both benzyl benzoate and turpentine are contact poisons and, as has been shown previously, the mite is killed soon after contact.

As the action of the two drugs, benzyl benzoate and turpentine, is closely similar, their mode of application on the body should also be on similar lines. As the mites are quickly destroyed, it is immaterial how long the emulsion is allowed to remain on the body. We have not yet come across any unpleasant reaction following its use.

Our experience of the treatment of scabies, is yet limited but the uniformly good results, we have obtained, justify its trial on an extensive scale in order to enable us to judge its true merit as a sarcopticidal drug.

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#### THE WASSERMANN-POSITIVE RATE OF CASES FROM HOSPITALS AND VENEREAL CLINICS OF CALCUTTA IN 1939, 1943 AND 1944

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THE intention is to present the findings in 6,000 cases with a view to determining if there is an increase in the incidence of syphilis in Calcutta. Groups of 1,000 cases have been taken serially from the Wassermann register of the laboratory.

#### THE TABLE

*The cases tested.*—The accompanying table gives the WR positive rate of a certain section, syphilitic suspects, of the civil population of Calcutta. It is by no means the positive rate for the mixed unselected population.

The bloods for examination were received from general wards in hospitals and venereal clinics. The general wards predominated before the anti-venereal drive, towards the end of 1943, and the clinics after the drive. Both from the hospitals and clinics the bloods were tested on clinical suspicion, not routinely. Only a small general hospital and a smaller special hospital were testing the bloods routinely.

The civil population of Calcutta was believed to be over 1½ millions in 1939 (1931 figures: 1,485,582 including Howrah and 1,196,734 excluding Howrah). The census of 1941 proved it to be over 2 millions (2,488,183 including Howrah and 2,108,891 excluding Howrah). The ration cards issued towards the end of 1943 proved it to be 3 millions (including Howrah).

By far the majority of the population tested was Indian.

*The periods.*—I and II represent the usual state of things in 1939. Two contiguous series are given to bring out the variation inherent in random samples under study.

III represents the slackest period. The number of bloods received per day is the lowest on record since 1939. This is due to the reduction in the ward accommodation.

IV represents the period immediately before the anti-venereal drive. III and IV may be considered together, like I and II or V and VI, for the same reason.

V and VI represent the usual state of things after the anti-venereal drive. Two contiguous series are again given to bring out the variation inherent in random samples of the item under study.

#### THE TECHNIQUE

The technique based on method no. 4 of the Medical Research Committee (British, 1918, now Council) has been summarized previously in this journal (Greval, 1943). The only feature worth repeating is the +++ reaction termed 'strongly positive'. For the purpose of obtaining it, the usual 1 in 5 dilution of the serum is put up with 4 MHD of complement and 1 in 15 uncholesterinized antigen. A complete inhibition of hæmolysis is +++. When a trace of hæmolysis is observed it is recorded T but reported +++. An advanced hæmolysis is recorded  $\pm$  but ignored altogether in reporting. All sera positive with uncholesterinized antigen are fully positive with the cholesterinized antigen as used in the original method.

The reaction, given typically by cases of secondary syphilis, is (i) almost independent of variation in complement, etc., and, therefore, not

likely to be affected by slight maladjustment in the reagents, (ii) more indicative of syphilis than ++ or + which do arise from numerous causes in the tropics much more frequently, and (iii) indicative of an infection which is neither too recent nor too old. The writers base their unbelief in the increased incidence of syphilis in Calcutta during the last five years on this reaction mainly.

#### OBSERVATIONS ON THE TABLE

*Has the incidence of syphilis increased in Calcutta during the last five years?*—A comparison of figures for 1939 and 1944 shows a decided increase in the total positive reactions per thousand and also in the strongly positive reactions per thousand. Besides, the thousand suspects could be collected in the latter year in less time. It begins to appear that the incidence has arisen.

When the position, however, is reviewed comparatively with (i) publicity of the anti-venereal drive, (ii) new provision of free test and free treatment of the anti-venereal drive, (iii) increase in population, and (iv) the unaltered relation between the strongly positive reactions and the total positive reactions, the question arises whether the rise is real or only apparent. The first three factors cannot fail to add to the figures considerably, *without any rise in the incidence of the disease at all*: there are more people in Calcutta, and they pay more attention to the disease. The fourth factor rather supports this opinion: if amongst the total positive cases, the number of cases which are neither too recent nor too old is relatively the same to-day as it was five years ago, then the infection must be occurring at the old rate;

A TABLE SHOWING THE WASSERMANN POSITIVE RATE OF CASES FROM HOSPITALS AND VENEREAL CLINICS OF CALCUTTA IN 1939, 1943 AND 1944

Periods	Number of cases tested	Positive reactions, all grades (+, ++ and +++)		Strongly positive reactions (+++ only)	
		Actuals	Percentage of the total	Actuals	Percentage of positive reaction
In 1939 :					
I. 11-4-39 to 8-5-39, 15 working days ..	1,000	146	14.6	55	37.7
II. 9-5-39 to 3-6-39, 16 working days ..	1,000	204	20.4	57	27.9
In 1943, before the anti-venereal drive :					
III. 2-1-43 to 23-2-43, 34 working days ..	1,000	235	23.5	91	38.7
IV. 23-7-43 to 29-8-43, 25 working days ..	1,000	275	27.5	51	18.5
In 1944, after the anti-venereal drive :					
V. 22-2-44 to 13-3-44, 13 working days ..	1,000	337	33.7	121	35.9
VI. 14-3-44 to 30-3-44, 10 working days ..	1,000	351	35.1	104	29.6



in other words the incidence per thousand in 1944 must really be the same as in 1939, although from the actuals it appears to have increased.

That circumstances like the present ones prevailing in Calcutta increase sexual irregularity which increases the incidence of syphilis cannot be denied. It is quite possible, however, that the static social elements in the civil population of Calcutta, that lend themselves to the irregularity, are almost exclusively in contact with the shifting population and thus do not affect appreciably the bulk of the static population. Social traditions and economic considerations convert this possibility into a probability.

*Incongruity of periods III and IV.*—The increase in the positive rate in 1943 can be, at least partly, due to more attention given to selection, consequent on the reduction in the number of patients in hospitals, consequent in its turn on the reduction in accommodation. The thousand suspects were collected in 25 to 34 days in 1943, as opposed to 15 to 16 days in 1939. The marked drop in the +++ percentage of period IV may be a vagary of random sampling.

#### LOW WR POSITIVE RATE OF AN UNSELECTED POPULATION AND MILDNESS OF THE DISEASE

Further observation will also decide whether there is an increase in the incidence of syphilis.

WR positive rate, indicative of syphilis, of the senior writer (Greval and Sen, 1942), for the unselected Indian population of Calcutta, is under 5.3 per cent. Whether this rate will be found to be higher after the war remains to be seen. A rise in the rate would be in favour of an increased incidence.

Syphilis in India does not thrive and therefore does not play the same havoc with the human body as in Europe. Whether the disease will become more virulent also remains to be seen. An increase in virulence will be indicative of an entry into the Indian syphilis of new strains.

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### REPETITION OF THE WASSERMANN REACTION

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THE intention is to draw attention to (i) the occasions on which a repetition is necessary, (ii) certain preparatory measures, and (iii) the Wassermann 'obsession'.

### OCCASIONS ON WHICH REPETITION IS NECESSARY

#### For diagnosis

(a) *When a suspicious primary lesion exists, and the first report is negative or doubtful.* If the treponema cannot be found, the reaction must be repeated fortnightly or weekly for 3 months from the date of the exposure. Diagnosis and treatment must be postponed. Otherwise the patient may have to submit to a lengthy treatment and life-long anxiety on suspicion alone.

If the risk has been taken with a partner who has later shown definite signs of primary or secondary syphilis, repeated clinical examinations and blood tests must be again continued for 3 months from the date of the exposure. Early primary lesions may be difficult to exclude in the female.

(b) *When a case with equivocal signs of late syphilis has given a negative or doubtful reaction.* Further observations are obviously necessary, including blood tests.

It is not very well known that 'for no apparent cause the bloods of 30 per cent of the patients slowly revert to negative, even though they may show definite signs of syphilis during this period' (Becker, 1937). As a matter of fact 'it is in these cases that persistently weakly positive reactions are found'.

(c) *When syphilis of the nervous system is suspected.* The CSF is also to be tested with or after the blood.

(d) *When other conditions (febrile diseases in general, and certain tropical diseases in particular) known to give rise to a false positive Wassermann reaction are present.* The reaction is repeated after the conditions have abated. The writer has listed the conditions previously (Greval, 1943). His own contributions to the list consist of: (i) kala-azar, (ii) leucithinophile eosinophilia and (iii) leucithinophile hepato-gastro-intestinal syndrome.

Latterly a post-vaccination period of 4 months has also been held responsible for false positive reactions of syphilis (Lynch, Boynton and Kimball, 1941; *Jour. A. M. A.*, Editorial, 1943; Venkataramanah, 1944). These false reactions appear to be obtained mostly with the flocculation test.

(e) *When a treated woman has become pregnant.* The slightest departure from the negative reaction is important in the interest of the offspring, for those who do not treat every pregnant woman with a mere history of syphilis.

Women tolerate the disease much better than men, probably because of the chemical changes associated with the menstrual cycle and especially the changes associated with pregnancy. It has been noted that repeated pregnancies tend to cure the disease in women and to prevent serious nervous complications, especially if pregnancy occurs in the first few months of infection' (Becker, *loc. cit.*).

(f) When a positive or doubtful Wassermann reaction has been found accidentally in an otherwise healthy subject, such as a donor of blood. Latent syphilis must be excluded by further tests of blood and CSF.

The writer's figures for latent syphilis in Indians, very much lower than those of previous writers, are:—

Crude rate (found initially) . . . 8.7 per cent.  
Corrected rate (persisting finally,  
without anti-syphilitic treatment) . . . 5.3 per cent.

These figures were obtained from the Indian population of Calcutta not yet affected by the Second World War. In the country the rate must be much lower.

(g) When a positive Wassermann reaction is not compatible with one's judgment of the patient's character or heredity.

#### For treatment

When the blood is tested as a measure of the treatment. A fall in the degree of fixation of the complement will indicate (i) whether the drug selected is making an impression on the system of the patient at all, and (ii) whether enough treatment has been given. Both indications are important: one may be dealing with conditions in which reaction and poisoning are feared and therefore the mildest remedies are used, as in cardiovascular disease, hepatic disease, advanced age and pregnancy; or one may be dealing with resistant cases and tough constitutions, and heroic measures may be needed.

The writer records the fixation in accordance with method no. 4 of the Medical Research Committee (1918, British, now Council) with two additions: (i) a reaction of +++ is recorded when uncholesterinized alcoholic heart extract antigen fixes 4 MHD of complement and (ii) a T (=trace of lysis) is recorded (ordinarily reported +, as long as the next lower reaction is +). The full range of the record is as follows:—

1	+++	} Positive, strongly.
2	++T	
3	++	} Positive.
4	+T	
5	+±	} Positive, weakly.
6	+—	
7	TT	} Doubtful. These reactions are not
8	T±	
9	±±	} 9/10–5/10 positive.
10	±—	
11	—?—	} Negative.
12	— —	

The utility of such a range in comparing repeated reactions is obvious. The expected and observed reactions of the titrated positive controls (Greval, Chandra and Das, 1940; Greval, 1944) on the same day are also available for deciding whether a slight change is significant.

Further, the writer uses two extra antigens (Bordet's cholesterinized antigen routinely, and McIntosh and Fildes' phenolized antigen for special cases) reactions with which extend the comparison. These reactions are recorded but not reported ordinarily.

Negative WR at the end of a 'course' but after an 'interval' is the aim of treatment. Several courses

may be necessary to attain this aim. Some extra treatment is then given.

Cases are known in which all treatment fails to influence the WR. When after a long treatment, suitably given, the WR is still positive, suspension of further energetic treatment is justified if (i) the CSF is negative and normal and (ii) the cardiovascular system is sound or if (iii) the patient is elderly.

#### For test of cure

When a cured case is being tested periodically. The length of the intervals varies with the physician's confidence in his treatment and with the patient's financial status, from 3 to 6 months. The total duration of the periodical tests also varies with the purpose: 2 years after suspension of treatment, as a rule; 5 years after infection, for marriage (in the male, can be shortened by treatment to 4, *vide infra*); and whole life for general observations. The whole life repetitions may be annual.

As to the minimum period of subsequent observation, an analysis of the result of treatment of early cases at the St. Thomas' Hospital V. D. Centre showed that by far the majority of relapses occurred within 6 months following suspension of treatment, that relapses in the second year were very uncommon, and were very rare after the end of 2 years. The minimum for early cases should, therefore, be 2 years' (Harrison, 1931).

The above remarks apply to blood only. The CSF also 'should be tested during the fourth and tenth year. The first is the end of the period when the changes found in early syphilis have disappeared in a proportion of cases. The second examination is best calculated to catch those cases where the fluid, having been rendered normal, has relapsed' (Ravant, quoted by Harrison, *loc. cit.*).

The seasonal variation in the Wassermann reaction (Hoverson *et al.*, 1935) and in the quality of the complement of the guinea-pig serum on which so largely depends the degree of fixation (Greval, Chandra and Das, *loc. cit.*; Greval, *loc. cit.*) are vital considerations. If possible, the repetitions should be made in the same season (or seasons).

#### CERTAIN PREPARATORY MEASURES

*Food before giving blood.*—The ideal time for giving blood for the test is early in the morning before taking any food. After that, any time before the heavy meal of the day ('morning' meal and lunch) will do. If this precaution has been ignored for the first test, it should be taken for the second and recorded.

Cloudy chylous sera are on the whole unstable, and more likely, therefore, to give a false positive (or doubtful) reaction.

*Withholding of protein diet for 3 days.*—A recent advance in the serology of syphilis (Barnes, Borts, Miller and Spanswick, 1943) advocates withholding all animal protein for 3 days before retesting the blood. The subject

under test is put on 'a milk-free, meat-free diet, with fresh vegetables and fruit juices *ad lib.* and six to eight glasses of water daily for 3 days'.

The writer has tested this plan in a short series of cases, and in some Indian patients (strict vegetarians) withheld *wheat* and *pulses* also. He has obtained definite quantitative reduction and at least one qualitative change in the doubtful reactions of some cases. The plan may differentiate between specific and non-specific cases when clinical examination and history fail. It is worthy of trial.

**Provocative injection.**—The writer is against the use of this measure (Greval, Chandra and Das, 1939; Greval, 1943). It is as likely to provoke a non-specific reaction as a specific reaction, and in India the causes of non-specific reactions are many. Very recently, the use of the provocative injection in the military hospitals has been given up in the diagnosis of early syphilis.

#### THE WASSERMANN 'OBSESSION'

Cases presenting themselves again and again for blood tests and also going for treatment from physician to physician are frequently encountered. Their attention should be drawn to the following facts and conclusions:—

(1) *False positive Wassermann reactions are quite common in India.* All conditions known to be responsible for them should be excluded before a lapse in the more or less remote past is accepted as the starting point of syphilis.

(2) *Syphilis does not play the same havoc with the human body in India as in Europe.* Late and intractable effects of the disease are borne by very few victims indeed. GPI is a rarity against '500 to 700 cases treated yearly since 1927' (Editorial, *Brit. Med. J.*, 1938) in England. Tabes is almost as rare, at least the typical case. Cardiovascular diseases exist but, excepting the aortic disease, their victims are found living useful lives, almost approaching the normal, with care.

If syphilis in India were not so tame, the country, consisting as it does of masses whose buying power (including procuring of appropriate treatment) is so low, would not have shown such increases in population at each census, even though the social conditions minimized the incidence of the disease.

(3) *The possibility of the involvement of the nervous system and the cardiovascular system can be excluded by the detailed examination of the CSF and the heart.*

(4) *A syphilitic male is not likely to infect his wife or offspring, 5 years after the infection, regardless of the treatment or cure, even in Europe.* In India probably the same happy immunity is available earlier.

(5) *A woman stands syphilis much better than a man, even in Europe.* In India her chances of curing herself by her own biochemistry must be better.

(6) *An infected expectant mother treated in the first half of the pregnancy can have a healthy offspring.* Again, chances in India must be better.

#### SUMMARY

1. *Repetitions of WR* are necessary for diagnosis, treatment and test of the cure. Non-syphilitic morbid conditions which are many in India, must be excluded. A detailed record of the reaction can provide a comparison. A seasonal variation occurs.

2. *Preparatory measures.* The blood is best given in the morning before taking food. Certain non-specific reactions decrease when animal protein is withheld from food for 3 days. Provocative injection is useless.

3. *The WR 'obsession'* of many patients should be resolved by optimistic reasoning. The optimism is justified. Syphilis does not thrive in India as it does in Europe.

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#### MALARIA IN INFANTS

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WITH a view to roughly calculating the period when mosquitoes are infective in the field, we register all the infants born on the estate and record the date when they develop fever for the first time within their first year. The analyses of the figures thus recorded, which extend over a period of five years (April 1936 to March 1941), may be of some interest. Malaria has been confirmed in each case by the microscope.

CHART 1

Age

Total number of births within the period (5 years)	Number infected within :—												Total number infected
	1st month	2nd month	3rd month	4th month	5th month	6th month	7th month	8th month	9th month	10th month	11th month	12th month	
349	1	8	19	7	4	5	5	6	6	3	4	3	71

CHART 2

Time of infection

Total number of births within the period (5 years)	Number infected in :—												Total number infected
	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	
349	1	6	10	12	8	18	1	3	1	..	3	8	71

CHART 3

Rainfall in inches (average for 5 years)

April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.	Mar.	Total
7.75	16.77	17.96	12.43	11.76	10.82	6.30	1.38	0.04	0.13	1.05	2.33	88.72

Chart 1 shows that the highest number of infants (19) were infected in the third month of their life. Chart 2 shows that cases occurred practically throughout the year, the highest number (18) being in September. No case occurred in January.

Thanks are due to Dr. C. Strickland, M.D., who suggested the plan and to the Malariologist, Central Laboratory, Madabpore, who examined the blood films.

## A BUTYL ACRIDINE DERIVATIVE IN 'INTESTINAL GIARDIASIS'

### A PRELIMINARY NOTE

By A. N. BOSE

J. K. GHOSH

and

P. C. RAKSHIT

(From the Bengal Immunity Research Laboratory, Calcutta)

DURING the investigation of the action of butyl acridine on human malaria, a few cases of intestinal infection in man were encountered with *Giardia*, and it was considered worth while to try its effect on such infection. Three cases were treated, the adult dose being 30 mg. three times a day for five consecutive days. The stools were carefully examined for the presence of trophic and cystic forms of the parasite before

the administration of the drug. During treatment and for a considerable period after treatment stools were repeatedly searched for the recurrence, if any, of the infection. All the three cases were completely cured. No relapse was encountered even in 6 months. The parasites disappeared by the third day after the commencement of treatment. Details of the cases are reported below :—

Case 1.—M. C. M., Hindu male, aged 28 years. Complaints of frequent attacks of diarrhoea for the last five years, indigestion, loss of appetite, flatulence, vague pain in the abdomen. Had been treated by his village doctor with emetine but had no improvement. On palpation of the abdomen nothing could be detected. Stool was examined, and numerous trophic forms of *Giardia* were seen. Butyl acridine was given in the doses mentioned above. The patient has been free from any trouble for the last 6 months. Stool was frequently examined for 6 weeks after treatment; no cysts or parasites were found.

Case 2.—S. B. S., Hindu female, aged 25 years. History of abdominal colic, for about 12 years' duration; in the right hypochondriac region, comes on twice or thrice a month. Discomfort in the upper abdomen after food; aerophagy. Always passes mucus with stool. Had various treatments with no benefit. Stool examination revealed both cystic and trophic forms of *Giardia*. Butyl acridine treatment was given. The patient was under observation for 3½ months with frequent stool examination. She is free from symptoms.

Case 3.—P. N. S., male child, aged 5 years. History of indigestion and ill health for three years. Stool sometimes loose, sometimes solid or semi-solid; disinclination for food. Poor physique. Had been previously treated with vitamins and other drugs. No improvement followed. Stool examination revealed enormous number of trophic forms of *Giardia*. Butyl

acridine was given 15 mg. thrice daily for 5 days. Subsequently stool was examined at frequent intervals for 3 months and was free from parasites. The health of the child improved remarkably; the appetite increased, and he gained in weight considerably.

## SEASONAL VARIATION IN CRIME\*

By RAJYASEVANIRATA C. O. KARUNAKARAN  
and

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### *Introductory*

In the study of crimes and criminals, their close association with pathology has received increasing recognition in recent years. Pathology is unbalanced or disordered physiology.

The normal physiological harmony of the various organs governs to a large extent the social conduct of the individual. Under the stress of famine and starvation, parents may leave their children on public roads to the mercy of strangers, or throw them into rivers and tanks. If newspaper reports are to be believed, during one of the severe famines in North China fifteen years ago, parents even slaughtered and ate their children. Instances are numerous of hungry and tired men, on their return home, getting irritated for trivial reasons—reasons which they would ordinarily ignore—and that irritation occasionally ending in violence and bloodshed. A well-disciplined person might become short-tempered when he suffers from fever or headache. The influence of intoxicants and drugs such as cocaine on human actions is so well known as to need no special mention here.

Among the factors which influence social conduct, the importance of environment has generally been accepted. 'Environment is the sum-total of the social, financial and psychological factors which surround the individual and may lead him to instability or stability in his personality, and may interfere with his nutrition and physical condition' (Cardwell 1940). In support, the same author quotes the words of King Lear:

'We are no longer our true selves

When nature, being oppressed, commands the mind

To suffer with the body'.

'Affects give energy to mental experiences and their influence extends through all psychological functioning. They influence the course of many physical functions. On the other hand they themselves are influenced by physical conditions within the body', writes Barrette (1926). Since physical conditions within the body are influenced by physical conditions outside it, 'affects' (feelings) which govern psychological functioning cannot be left uninfluenced by external physical forces.

The influence of meteorological conditions on health and sense of well-being has long been realized by authorities on public health. One of the admitted causes of accidents in factories is the high temperature and humidity inside the work rooms which make the workers lose their sense of judgment and precision; and persons who have to work under such conditions are given shorter shifts than others.

Want of concentration, peevishness and irritability are the common experience of everyone on sultry days. The influence of season on human emotions and actions has been fully understood by poets of all countries, who have immortalized the glory of the spring in their verses. Poets and scientists have noted and described the influence of season on plants and lower animals; but, so far as we are aware, they do not seem to have paid attention to the influence of season and climate on emotions and actions which culminate in crimes.

### *Present study*

The authors in the course of their medico-legal work found that year after year the distribution of cases showed some correlation with the season of the year. A study of this subject therefore appeared interesting. The average quarterly incidence of crime—murder, culpable homicide not amounting to murder, and sexual offences—has been calculated for the last 11 years (1932-1942) and separately for the last 3 years. The average maximum and minimum temperature, as well as humidity for each quarter of the last 3 years, has also been calculated from the records of the Observatory at Trivandrum. The results of this study are shown in tables I and II.

### *Discussion*

The quarters are calculated on the basis of the official Malabar year. Being a coastal country, the climate of Travancore is more or less equable, and wide variations of temperature do not occur. But the first and the last quarters (September to November and June to August) are generally the cooler periods of the year, and the third quarter is the hottest. A larger number of cases requiring medico-legal investigation has been reported during this quarter every year than in other quarters, and the averages for the past 11 years also show this difference. The maximum and the minimum temperatures of this quarter are only 4° to 5° higher than that of the first and fourth quarters; but the discomfort, lassitude and irritability experienced during this season is much greater than this difference in temperature might indicate, and would make one recall King Lear's words, 'When nature being oppressed . . . ' etc. A general correlation between the higher temperature and increase in crime is clear from tables I and II. No correlation exists between

\*A paper presented before the Indian Science Congress, 1944.

TABLE I  
Seasonal variation in crime

Quarter	Months	1939-40				1940-41				1941-42				Average number of crimes based on the statistics for 11 years from 1932-1943
		Average temperature		Relative humidity	Number of crimes	Average temperature		Relative humidity	Number of crimes	Average temperature		Relative humidity	Number of crimes	
		Maximum	Minimum			Maximum	Minimum			Maximum	Minimum			
I	September, October and November.	86.9	74.6	81.0	23	86.2	74.6	84.2	29	86.7	74.1	78.9	29	29.6
II	December, January and February.	88.3	73.7	66.8	22	89.7	73.8	72.0	51	89.2	72.5	70.0	34	37.1
III	March, April and May.	89.1	78.6	73.5	30	90.7	77.6	76.9	75	90.1	76.8	76.5	46	40.6
IV	June, July and August.	84.4	74.6	86.0	23	85.6	74.9	84.9	28	84.6	74.1	85.2	30	31.0

TABLE II

Monthly incidence of crime falling under the category of murder, culpable homicide, sexual offences (mainly rape) received during the period 1932 to 1943.

Serial number	Year*	I QUARTER				II QUARTER				III QUARTER				IV QUARTER				REMARKS
		August to September	September to October	October to November	Total	November to December	December to January	January to February	Total	February to March	March to April	April to May	Total	May to June	June to July	July to August	Total	
1	1942-43	9	11	10	30	8	14	10	32	18	21	15	54	5	9	14	28	The highest monthly average is from March to May.
2	1941-42	10	12	7	29	11	11	12	34	19	12	15	46	7	16	7	30	
3	1940-41	8	7	14	29	16	17	18	51	14	29	32	75	12	11	5	28	
4	1939-40	12	4	7	23	9	9	4	22	5	16	9	30	7	10	6	23	
5	1938-39	2	14	9	25	17	9	19	45	11	17	13	41	12	18	9	39	
6	1937-38	10	8	20	38	13	10	20	43	7	10	11	28	9	9	10	28	
7	1936-37	11	7	9	27	16	10	17	43	4	12	13	29	19	4	10	33	
8	1935-36	8	12	7	27	15	5	12	32	11	16	12	39	17	12	10	39	
9	1934-35	14	10	7	31	14	15	17	46	11	13	14	38	13	5	9	27	
10	1933-34	18	3	8	29	6	14	11	31	8	11	10	29	13	7	17	37	
11	1932-33	6	14	17	37	10	10	9	29	12	6	20	38	8	11	10	29	
Average		9.8	9.3	10.5	29.6	12.3	11.3	13.5	37.1	10.9	14.8	14.9	40.6	11.1	10.2	9.7	31.0	

\* The Malabar year begins from about the middle of August.

the average humidity and distribution of crime. The quarters which show a higher humidity and lower temperature are the periods of the year when there is a feeling of greater comfort.

The second and third quarters of the year are relatively periods of plenty in food and money; and the first and fourth are periods of scarcity. Economic factors do not therefore appear to be responsible for the noted variation in the incidence of crimes,

Also no correlation is found between freedom from employment and the incidence of this class of crimes, because of the four months of comparative leisure among the ryots, two fall in the fourth quarter, one each in the first and the second quarters and none in the third quarter which has the highest number of crimes (*vide* table II).

The only factor which seems to have a bearing on the observed variation appears to be the



temperature. It might be interesting if similar studies be carried out in countries where the seasonal variations are more marked.

### Summary

The seasonal distribution of cases of homicide, culpable homicide not amounting to murder, and sexual offences investigated medico-legally by the authors during the last 11 years has been studied.

The seasonal variation in temperature and humidity has been calculated.

It is found that there is some correlation between the incidence of crime and rise in temperature. No such correlation is found with reference to humidity.

The period of the year with the maximum temperature is relatively the period of plenty; and so economic factors do not appear to be responsible for this difference in the distribution of crimes.

The seasonal variation in temperature is not more than 6°, but the hottest part of the year is the most oppressive period.

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## FORMIC AND ACETIC ACIDS AS POISONS\*

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### Historical

THE appearance of the volatile fatty acids, formic and acetic, in toxicology is very patchy. According to Autenrieth (1928) formic acid

Although acetic acid has been used for suicide, and accidental poisonings have also been fairly common in certain countries of Europe, notably Russia and Germany from the beginning of the present century, Autenrieth (1928) and Owens (1935) have not mentioned any instance of poisoning with this acid. This might be because, as Hunt and Gettler say, 'in the United States and England, poisoning by acetic acid seems to be rare'. There were according to these authors 4 fatal cases in England and Wales in 1912, while in Germany there were 256 cases of acetic acid poisoning in 1909 and in St. Petersburg in 1908 it accounted for 34 per cent of all suicides and 72 per cent of all cases of poisoning. Blyth and Blyth (1920) refer to 12 cases as having occurred in England and Wales during the five years ending in 1916. Two instances of cases of acetic acid poisoning have been mentioned in the Annual Report of the Medical Officer of the Ministry of Health, 1937. Fifteen cases have been reported from Ceylon during 1931-42 (*Analyst*, 1932, p. 575; 1937, p. 469; 1938, p. 501; 1939, p. 512 and 1940, p. 652).

Owens (1935), while stating that 'a few fatal cases of poisoning by this have been reported as having occurred in Europe', does not mention a single case anywhere in India. It has been referred to as poison only once during the last decade by the Chemical Examiner to the Government of Madras (Annual Report of the Chemical Examiner's Department, 1940, p. 15).

### Cases in Travancore

The number of cases from which we have been able to isolate formic and acetic acids during the last seven years is significant and interesting. Although toxicological analysis was introduced in Travancore 51 years ago, these acids had not figured in our toxicological history prior to 1936. Since then we have had 71 cases out of a total of 428 cases of poisoning distributed as follows:—

	1935-36	1936-37	1937-38	1938-39	1939-40	1940-41	1941-42	1942-43	Total
Formic acid ..	..	6	8	13	5	2	..	..	34
Acetic acid ..	7	1	3	1	5	11	6	3	37
Total ..	60	54	47	55	53	64	51	44	428

has 'hardly ever come up as poison'. Five cases have however been reported from the Federated Malay States (*Analyst*, 1940, p. 459), 4 from the Straits Settlements (*Analyst*, 1937, p. 742; 1939, p. 744), and 2 from Ceylon (*Analyst*, 1932, p. 575) during the period of 1931-42.

The regional distribution of these cases is significant. Administratively the State is divided into three districts, and in one respect the districts are strikingly different from each other.

Travancore is the biggest rubber producing area in India. Of the 136,605,671 acres under rubber in India, 10,446,517 acres are in Travancore. But the distribution of rubber among the districts is unequal. Trivandrum division has little rubber. Although both Quilon and

\*A paper presented before the Indian Science Congress, 1944.

Kottayam have extensive acreage under rubber, most of the small holdings are in the Kottayam district. Of the 71 cases under review, Kottayam claimed 62, Quilon 9 and Trivandrum none.

The close association of rubber with poisoning by the two acids is remarkable. Indeed, it is the development of this industry that has brought these acids into common use in this country and led to their deliberate or accidental use as poisons. The high incidence of such cases in Ceylon and Malaya, two of the leading rubber producing countries of the world, corroborates this view.

During the last two years, there has been no case of poisoning by formic acid because the outbreak of war has made it unavailable. Acetic acid has also become increasingly costly and more difficult to obtain, and it is to a large extent replaced by a sulphuric acid preparation called 'Sulpholux'. Because these acids have become more precious, the owners are naturally taking greater care of their stocks than they did before.

The 71 cases come under three heads: (a) suicidal, (b) accidental, (c) overdose—when deliberately taken as a medicine.

	Suicidal	Accidental	Overdose	Total
Formic acid ..	27	6	1	34
Acetic acid ..	28	7	2	37

No case of homicidal poisoning has been reported, obviously because they do not satisfy the primary properties which criminals desire in their poisons—i.e. smallness of dosage and absence of unpleasant smell and taste. The choice of a poison for suicide is governed by its easy availability as well as by the level of intelligence of the victim. An intelligent person's suicide is seldom a momentary impulse. It is generally the result of long thought and brooding, and a quick-acting poison not likely to cause much agony, such as the cyanides, opium or arsenic will be preferred. In the case of an illiterate labourer, the thought of suicide is often a sudden impulse, following, say, a domestic quarrel, discharge from employment, etc. He has neither the knowledge of the more powerful poisons nor the cunning or means to procure them. He uses what he can easily get and is not deterred by fear of suffering. This explains the large use of these acids for suicidal purposes in this country. Their extensive use in the rubber industry made them available to anyone, and the victims invariably belonged to the lower strata of society.

A parallel to this can be found in the use of acetic acid for suicide in Russia and Germany during the early part of this century, referred to above. Essence of vinegar containing 80 per cent of acetic acid had just come into use as

a food preservative, and was freely available to all, and the poor people, probably not more advanced in intelligence than the labourers engaged in the rubber industry, used it for suicide.

Accidental consumption of any poison is due to its domestic storage along with receptacles containing medicine or alcoholic drinks. Accidental poisoning by carbolic acid and other disinfectants has often occurred in Great Britain in this manner, and by acetic acid in Germany and Russia. In Travancore, while no domestic storage of these acids is done in the large rubber estates, the small holders keep small quantities at home in bottles similar in size and appearance to those used for keeping various indigenous medicines or alcoholic drinks. The smell of some of these indigenous preparations is not very different from that of these acids, and this leads to accidental poisoning.

Although the conditions under which acetic and formic acids have been used for suicide or consumed accidentally are more or less similar everywhere, there is another group of cases which, although small, is of a unique type. In these cases the victims were reported to have been using small doses of acetic acid for the relief of their stomach pain. It may be noted here that the incidence of gastro-duodenal disease in Travancore is estimated to be 3 to 4 times that of other parts of India (Orr, 1936) and occasionally larger doses of acids than usual have been consumed either accidentally or deliberately with the hope of getting the relief which smaller doses had failed to give. In a fair proportion of suicides also, the desire to escape for ever from their incurable gastric pain appears to have been the motive for the crime.

#### *Signs and symptoms*

These are in general similar to those caused by mineral acids. The post-mortem appearances are also of the same nature. Vomiting, salivation and a burning sensation of mouth are present invariably. The vomit contains bloody fluid. The victim usually rolls about in agonizing pain. The pulse becomes rapid first and then slows down. Respiration also follows the same course of rise and fall. The skin is often cold and the face cyanosed, and there is rattling of the throat and irritation of the respiratory passages, although in the majority of cases the larynx and trachea were found normal. If concentrated acid is taken, the whole of the mouth and tongue may be corroded, the skin over the chin, front of the neck and on the upper part of the chest showing brownish desquamation if the acid has flowed down the mouth. Sometimes dark-stained streaks run down from the angles of the mouth and the middle of lower lip just under the chin, through the trickling down of the acid.

#### *Fatal period*

Death in acetic acid poisoning is stated to occur in 48 hours by Reid Hunt and Gettler,

We have reliable information about this point in 14 cases of formic acid and 21 of acetic acid poisoning, and this is given below :—

coagulates only 11 lb. of latex. In none of the cases of poisoning by formic acid did the victim survive; even 4 ounces of a 50 per cent diluted

		Deaths in less than 2 hours	2-4 hours	4-6 hours	6-12 hours	12-24 hours	24-48 hours	More than 48 hours
Formic acid	..	2	2	1	3	4	2	..
Acetic acid	..	1	2	4	4	6	1	3

Of the three victims of acetic acid who survived for more than 48 hours, one survived for 3 days, another for 7 days and the last for 14 days. The second was a young adult male (24) who had swallowed the acid with his stomach loaded with toddy.

#### *Post-mortem appearances*

They included the presence of blood-stained froth in the mouth and nostrils. The pupils were usually dilated. The right side of the heart was full with blood, and the left empty. The lungs were often congested and crepitant; in some cases they were normal. The liver, kidney and spleen were generally congested. If the concentrated acid was swallowed on an empty stomach, the latter was often distended and dark in appearance and contained dark thick fluid matter. With large doses the coats of the stomach had a dark and burnt appearance. This dark appearance was not noticed when the acid was taken on a loaded stomach. The coats might be normal, although a congested appearance was sometimes seen in such cases. If the dose was heavy enough, the intestines might also be dark in colour and distended in appearance. The bladder in formic acid poisoning cases was empty. This being so, examination of the urine which would have thrown light on the rate of absorption of the acid into the system and excretion could not be carried out. The membranes of the brain, the brain substance and ventricles were often congested, the latter containing sometimes cerebrospinal fluid. Death appeared to result from asphyxia.

#### *Quantities detected*

In formic acid poisoning the quantities detected have ranged from 0.04, 0.17, and 0.55 to 31.8 grammes of anhydrous acid, and in acetic acid cases from a trace to 2.20 and 2.40 grammes of anhydrous acid.

#### *Toxicity and fatal dose*

The two acids, being corrosive liquids, destroy the epithelial tissues, formic acid being more irritant than acetic acid. It may be noted here that in the use of the two acids for the coagulation of rubber, 1 ounce of formic acid is enough for 18 lb. of latex whereas 1 ounce of acetic acid

acid proved fatal. In two of the cases of acetic acid poisoning in which 2 ounces of undiluted acid were swallowed, recovery was seen. Death was however reported within 9 hours in a case in which the victim, a man of 35, took 2 ounces of the concentrated acid.

#### *Separation, detection and estimation*

For quantitative estimation of acetic acid, a known weight of the well-comminuted viscous (100 grammes) is taken in a litre flask with a long neck. 30 c.cm. of 25 per cent phosphoric acid is added, together with 200 c.cm. of water to make the volume up to 300 c.cm. A few glass beads are introduced into the flask. A still head is used and the distillation is conducted with vigorous boiling. The volume of the liquid is kept constant by adding distilled water drop by drop from a separating funnel, distillation being carried on until about 1,500 c.cm. of the distillate have passed over, when usually the point of neutrality to litmus is reached. Stir an excess of calcium carbonate with water and add to the distillate. Bring at once to the boil, and then evaporate in a flat dish on the water bath to dryness. Dry the whole residue for an hour at 100°C. Add 50 c.cm. of hot water, keep for a few minutes and filter, washing the dish several times with warm water and passing the liquid each time through the filter. Cool. Make up to 500 c.cm. A portion of this solution is evaporated to dryness on the water bath, dried at 100°C. and the residue is heated in a hard glass test tube with arsenious acid. The presence of acetic acid is inferred from the smell of cacodyl produced. The ethyl acetate test can be applied to a portion of the residue; but often the presence of organic matter prevents the smell being noted. In such cases, the cacodyl test answers the purpose very well.

Take 25 c.cm. of the above solution in a long-necked flask of 300 c.cm. capacity and proceed as follows: Add 30 c.cm. of water free from CO<sub>2</sub> and 10 c.cm. of phosphoric acid (sp. gr. 1.7). The volume of the liquid in the flask is kept constant by adding CO<sub>2</sub> free distilled water. The distillation is carried on for 1½ to 1¾ hours, the distillate being collected in a flask containing excess of a known volume of standard NaOH, to which access of CO<sub>2</sub> is prevented by providing a bent tube containing soda lime. Ninety-five per cent of the acid is evolved during the first hour. The excess of NaOH is titrated with standard H<sub>2</sub>SO<sub>4</sub>, using phenolphthalein as indicator. Each c.cm. of N/10 NaOH represents 0.006 grammes acetic acid.

For the quantitative estimation of formic acid, the method suggested by Autenrieth (1928) may be followed. The presence of organic matter interferes with the usual reduction test (with silver nitrate). This can be avoided if the residue is treated with magnesium and dilute sulphuric acid in a distilling flask, the contents distilled, and the distillate tested for formaldehyde by the usual reagents namely phloroglucinol and resorcinol (Henry Leffmann in Allen's *Commercial Organic Analysis*, Vol. I, 1924).

### Summary

Formic and acetic acids have figured in the toxicology of Travancore in a remarkable manner during the last 8 years. Prior to 1936 there were no recorded cases of poisoning due to these acids, but since then 71 cases have occurred out of a total of 428 cases in which poison was detected. Formic acid does not appear to have found a place in toxicology elsewhere in India, while acetic acid has been mentioned only once in the last decade by the Chemical Examiner to the Government of Madras.

The regional incidence of these cases shows their close association with the rubber industry, in particular with the distribution of the small rubber holders whose store room is a part of the house they live in. The scarcity of the acids resulting from the outbreak of the war has considerably reduced the incidence of poisoning by these acids.

In 77 per cent of cases the acids were swallowed for suicide; in 18 per cent it was accidental. There were no instances of their use for homicide, but in 3 cases death followed deliberate use for relief of stomach pain.

Death may occur within a few hours or up to 14 days after swallowing. While 2 ounces of the concentrated acid have been found generally fatal, in a few cases of acetic acid poisoning, that dose did not cause death. All cases of formic acid poisoning were fatal.

The signs and symptoms are those of irritant poisoning, and post-mortem appearances are suggestive of death from asphyxia.

The technique adopted by the authors for the qualitative and quantitative estimation of the acids is described.

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## ON THE EFFICACY OF 'BUTYL ACRIDINE' IN THE TREATMENT OF MALARIA

### A PRELIMINARY NOTE

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and

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*General.*—Recently it has been shown by Siddons and Bose (1944) that the compound

(2-chloro-7 methoxy 5 $\delta$ -diethyl-amino-butyl) amino-acridine, hereafter called the butyl acridine, was highly effective in controlling the infection of *Plasmodium knowlesi* in rhesus monkeys even in small doses. The same compound has previously been shown by one of us (Basu and Bose, 1941) to exert a considerably higher lethal effect on cultures of *Paramacium caudatum* than the corresponding amyl-acridine derivative commonly known as atebrin. Further as the anti-malarial action of compounds follows closely their effect on paramœcia (Kindler, 1938), it was considered to be of interest to study the effect of this drug even in smaller doses on human malaria cases.

*Experimental.*—A total of 27 adult cases of human malaria was studied in our out-door clinical department. The patients were all employees of the firm, and hence control during treatment was rigid, and each case was easily followed after treatment as long as it was necessary. Out of the 27 cases, 22 were of benign tertian infection and the rest of malignant tertian. Quartan cases were not encountered.

*Assessment.*—Immediately after admission, thick and thin blood films were examined for parasites to confirm the clinical diagnosis. After confirmation the patients were put on butyl-acridine treatment; 30 mg. thrice daily for 5 consecutive days was the usual routine treatment. An alkaline mixture containing sodium citrate and bicarbonate was also given along with the drug. A blood film of each case was examined daily for several days even after the blood became free from parasites and fever subsided. The urine of each case was examined during treatment to detect whether any unusual elements appeared.

*Results of treatment.*—The effect of treatment with butyl acridine was very hopeful. The parasites always disappeared by the third day, and the fever subsided. No untoward symptoms such as nausea, vomiting, headache and abdominal pain were noticed. The conjunctivæ were tinged slightly yellow in a small number of cases, undoubtedly due to the colouring nature of the drug. The urine was found to be normal in all cases except one in which some mucin appeared after administration. This, however, disappeared as soon as the drug was stopped.

During the follow-up of the treatment it was, however, noticed that relapses occurred in about 45 per cent of cases of vivax infection just as previously observed in the case with monkeys (Siddons and Bose, 1944). The remaining cases were apparently cured. The relapses occurred between the second and third week, and cases once having a relapse were subject to further relapses as well. Of course, the relapses could always be controlled by further administration of butyl acridine. Cases with no relapse for 3 months were taken to be cured.

In 51 cases of malignant tertian infection no relapse occurred up to a period of 6 months. Though the drug was effective in destroying the

trophozoites in the peripheral blood, it was found ineffective in freeing the blood from crescents which were, however, subsequently tackled successfully with another quinoline derivative prepared in this laboratory.

#### Analysis of the cases

Nature of infection	Number of cases	Number cured	Number relapsed	Percentage of relapse
<i>P. vivax</i> ..	22	12	10	45.5
<i>P. falciparum</i> ..	5	5	nil	nil

**Discussion and conclusion.**—It is the common observation of all investigators to come across relapses in cases of malaria, whatever drug might have been used in the treatment. Frequent relapses with quinine and amyl-acridine derivative (under the trade name atabrin) have been reported. The action of butyl acridine in doses employed by the authors is also no exception to such findings. Work has however been undertaken to find out the relative relapse rates with this compound at higher dosage and in comparison with amyl-acridine derivative. Certain indications during the course of this investigation suggested the possibility of reducing the relapse rate by giving other drugs in combination with this drug.

Our thanks are due to Dr. U. P. Basu for the keen interest taken in this work.

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## A Mirror of Hospital Practice

### A CASE OF TYPHUS FEVER COMPLICATING KALA-AZAR IN CALCUTTA

By P. C. SEN GUPTA, M.B. (Cal.)

Officer-in-Charge, Kala-azar Research Department,  
 Calcutta School of Tropical Medicine

THAT a fever of the typhus group occurs in Calcutta has been recognized only during the very recent years. In June 1942 there was an outbreak of typhus amongst some British soldiers stationed in Calcutta and of 16 patients 2 died (Napier, 1943). No clue as to the vector of infection could be ascertained. In the available literature there is a record of only one

case occurring amongst the civil population of Calcutta. Lowe (personal communication) had heard of an outbreak of fever, probably typhus, in the dock area of Calcutta, and has seen a number of cases among the military personnel.

The case that is reported below is in all probability the first recorded case of kala-azar in which typhus occurred as a complication during the course of specific treatment for leishmaniasis.

#### Case note

J., an Indian female child, aged 4 years, attended the kala-azar clinic on the 5th June, 1944, for continued fever, progressive weakness and emaciation for 3 months. On examination, the child was found to be thin and anæmic with accentuated pigmentation over the forehead and face and roughness of the skin and thinning of hair. There was well-marked pulsation of the carotids. The liver was enlarged 2 inches below the costal margin and the spleen 3 inches below the tip of the ninth left costal cartilage. The heart and the lungs did not show any abnormality.

The aldehyde and antimony tests and the complement-fixation test for kala-azar were positive, and the patient was diagnosed as a case of kala-azar.

The patient was put on specific treatment for kala-azar on the 8th June, 1944. She was given intravenous injections of aminostiburea twice a week. The first dose was 0.05 g., the second 0.10 g. and the rest 0.15 g. The patient became afebrile after three or four injections, and the course of injections was being continued. On the 26th July, she had an attack of high fever with pains all over the body, burning sensation over the limbs and headache. The fever was high for 5 or 6 days. On the fifth day of this attack of fever, a rash was noticed by the relatives of the patient. This was first noticed on the legs and by the next day on the trunk and both arms. The patient was seen on the 31st July. There was a low degree of fever, and there was seen a profuse dusky erythematous blotchy rash over the legs, a few erythematous patches over the arm and over the abdomen. No rash was seen on the face. No marked enlargement of the lymph glands or any small necrotic ulcer like that of tsutsugamushi was seen. The patient was treated symptomatically, and she made an uneventful recovery. The rash gradually disappeared, and on the 10th August, no rash was visible.

The child had almost completed her course of injections but there was still some enlargement of the spleen (1 inch), and she was still fairly anæmic. The patient is under observation, and it seems likely that a second course of injections will be required to complete the cure of kala-azar.

#### Results of Weil-Felix tests

Date	OX2	OXK	OX19
31-7-44	Neg.	1:400	Neg.
3-8-44	"	1:25	"
7-8-44	"	Neg.	"

#### Discussion

The clinical history—the type of fever and rash—indicates the probability of typhus fever. The Weil-Felix was positive in a significant titre to XK on the seventh day of illness. This confirms the diagnosis of typhus caused by a strain of rickettsia similar to that of tsutsugamushi fever. The results of the subsequent Weil-Felix tests were however unlike what is seen in an average case of typhus fever. It is



usual for the agglutination titre to rise progressively, and it is quite common to get a positive reaction in 1 : 2000 or even higher dilution at the end of a fortnight of fever. In this case the agglutination titre fell rapidly and by the fourteenth day of fever the reaction was negative in 1 : 25 dilution.

The reason for such anomalous Weil-Felix reaction is not far to seek. It is a well-recognized fact that a patient suffering from kala-azar or convalescent after the completion of the specific treatment, shows very poor immunity reactions. Napier (1927) pointed out that even when kala-azar followed bacteriologically proved typhoid fever the agglutinating property of serum rapidly fell as the patient developed kala-azar. Das Gupta (1943) found that on injections of leptospira vaccine there was no immunizing response in the vast majority of convalescent kala-azar cases.

This patient who had not even completed the full course of treatment for kala-azar and was probably still suffering from this disease when the complication, *viz.*, typhus fever, supervened. The indications were that the leishmanial infection was still active, and a second course of treatment would probably be required for its cure; the reason for the fall in titre of agglutination can thus be well understood. The antibodies are produced mainly by the cells of the reticulo-endothelial system, and visceral leishmaniasis is an infection which extensively and exclusively involves and practically blocks this system.

#### Summary

1. A case of kala-azar developed typhus fever during the course of specific treatment for leishmaniasis. This is in all probability the first recorded instance of a patient developing typhus fever as a complication of kala-azar.

2. The strain of rickettsia in this case that occurred in Calcutta is analogous to that of tsutsugamushi fever, a positive agglutination being obtained with proteus OXK.

3. Certain unusual features in the Weil-Felix test observed in this case are discussed.

#### Acknowledgment

The writer is thankful to Dr. G. Panja, Professor of Bacteriology and Pathology, Calcutta School of Tropical Medicine, for the reports of the Weil-Felix tests.

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## AN UNUSUAL CASE OF COMA

By B. M. KOTHARY, M.B., B.S.

Jodhpur

T., AGED 24, of good build, slightly anæmic, was admitted into the Windham Hospital for pain in the joints and some rash for three months.

There was nothing particular in his family or personal history; no history of any fits or nervous ailment was available. His Kahn test was strongly positive, and he was put on anti-syphilitic treatment. He was improving satisfactorily, the rash subsided, and the joint pains were gradually getting less. The second N.A.B. injection was given on the 11th March, 1944, without any reaction; and the third bismuth injection was given on the 15th March. He was well for two days. On the 17th at about 1 p.m. he went to the bath room and fell down with severe convulsions. He was brought to his bed, when examination showed that he was semi-conscious, was unable to speak, and was having convulsions at intervals. There was slight rigidity but no paralysis of any part of the body. The pupils were dilated and sluggishly reacting.

On the 18th morning, the patient had a temperature, rising up to 102°F. He was now completely unconscious and passing urine and faeces in the bed. Kernig's sign was doubtful, because the whole body was extremely rigid. The leg sign was absent and the pupils were very much dilated and not reacting. Blood examination did not show malarial parasites, and the differential count was normal. Urine examination did not reveal anything except a trace of albumin. Presuming that it was a case of cerebral malaria, 10 grains of quinine were injected intramuscularly. In the afternoon, lumbar puncture was done but nothing abnormal was detected on laboratory examination. Next morning, on the 19th, the temperature came down to normal, but his coma was as deep as before. The rigidity was as before, and the pupils were still dilated. Quinine was repeated intramuscularly and solusseptasine, 5 c.cm., was given intravenously later on, but his unconsciousness persisted uniformly till the evening when the patient had a forceful vomit containing a roundworm, about 10 inches long. Immediately after this, the patient complained of thirst and could speak slowly. On further questioning, the patient complained of vague pains in the body and slight weakness. The rigidity disappeared and the patient felt relieved. The nervous system was examined thoroughly, and nothing abnormal was detected. Since then the patient has been perfectly normal; he is taking the usual course of treatment. He was given 3 courses of santonin but no ova or worms were detected in the stools.

The unconsciousness in this patient was of unusually long duration (52 hours): its cause is not clear.

Thanks are due to Dr. J. N. Madan, Principal Medical Officer, Jodhpur State, for his kind permission to report this case.

## A CASE OF SYPHILIS OF THE STOMACH

By P. N. LAHA, M.D. (Pat.)

Department of Medicine, Medical College, Agra, U. P.

*Introduction.*—Syphilis of the stomach is regarded as a very rare condition. Till recent years, it was a matter of heated controversy particularly among clinicians, as to whether gastric syphilis ever occurred. In recent literature a fairly large number of cases have been reported. That it does occur is no longer a matter of controversy. In spite of recent contributions we must continue to look upon gastric



syphilis as a very rare condition. In 4,880 autopsies at Bellevue Hospital there were 316 examples of advanced syphilis but only 1 case of syphilis of the stomach; and in 13,000 autopsies at the London Hospital, Turnbull was unable to find a single undoubted case (Boyd, 1940). It is reported to be common in China and Russia.

**Pathology.**—Syphilitic infection of the stomach takes the form of an invasion of the submucosa, the usual histologic pathology characteristic of syphilis elsewhere in the body being present, that is, hyperplasia of the connective tissue elements, giant-cell formation, hyaline degeneration of the gummatous areas, endarteritis of blood vessels of the involved area, etc. (Tice, 1924). Gastric syphilis is one of the forms of chronic inflammatory gastritis. The gross pathologic picture of syphilis of the stomach is grouped under three forms—(a) a gummatous mass in the region of and involving the pylorus; (b) diffuse gummatous infiltration of the stomach in which secondary tissue formation may cause an hour-glass deformity of the ventricle of the organ; (c) a gummatous ulcer or multiple ulcers appearing on or about the lesser or greater curvatures and simulating in its course that of a benign ulcer.

**Clinical features.**—It affects males twice as frequently as females. The patient complains of epigastric pain usually immediately after meals but it may be delayed as in ulcer. Nausea, anorexia and anæmia are very uncommon but vomiting is fairly common. The patient seldom gets hæmatemesis, and occult blood is only occasionally detected in the stools. Eighty-five per cent of cases show achlorhydria and in most of the remainder there is hypochlorhydria (Price, 1942). A tumour is only occasionally palpable, and physical examination may reveal tenderness over the pyloric region or in the epigastric triangle. Other syphilitic manifestations may be present.

**X-ray picture.**—The following types are described (Shanks *et al.*, 1938):—

1. Generalized infiltration, producing a stomach markedly diminished in size, with rapid emptying and compensatory œsophagectasia. Peristalsis is diminished or absent. The condition closely simulates linitis plastica, and generalized scirrhus carcinoma.

2. The dumb-bell deformity, resulting from fairly symmetrical infiltration and contraction of the pars media. A large annular scirrhus carcinoma produces the same deformity, and this type is usually diagnosed as such.

3. Localized areas of infiltration and ulceration in the stomach. This type simulates a fungus carcinoma.

4. Localized pyloric and pre-pyloric infiltration, which tends early to produce stenosis. It produces a filling defect very similar to that of a scirrhus carcinoma.

The differential diagnosis between gastric syphilis and other lesions which it may simulate cannot be made on the radiological evidence.

The diagnosis of syphilis of the stomach is based on the finding of a positive Wassermann reaction and response to anti-syphilitic treatment. Gastroscopic investigations do not show any special features.

Treatment is the same as that followed in syphilis elsewhere in the body.

### Case report

K. A., Muslim male, aged 60 years, was admitted into the hospital with complaints of pain in the abdomen, chiefly in the epigastric region, felt a little while after meals, and occasional vomiting, duration one month. The onset was gradual.

**Examination.**—The patient was a thin old man, with normal temperature, pulse and respiration rates. He had a poor general health, but was not anæmic or jaundiced. The epitrochlear glands on both sides were fairly enlarged. There was tenderness in the epigastric triangle. The spleen and liver were not enlarged. His blood pressure was 117/80 mm. of Hg. Other systems revealed no abnormality.

**Investigations.**—Stool showed no parasites or occult blood. Gastric juice—complete achlorhydria; a few epithelial cells present; no lactic acid detected. W.R. was strongly positive. X-ray of the stomach showed diminished peristalsis and no other abnormality.

**Progress and treatment.**—A diagnosis of syphilis of the stomach was made. A full course of anti-syphilitic treatment with mapharside, bisglucol and iodide was given. He was completely cured of his pain and vomiting. After the completion of the treatment, his W.R. became completely negative; gastric juice showed presence of free hydrochloric acid; and gastric peristalsis as detected by x-rays was normal.

He was discharged cured from the hospital. A follow-up of the case has been done up till to-day (7 months), and he is perfectly well and looking much improved in general health.

### Summary

A description of syphilis of the stomach has been given in brief with an illustrative case report.

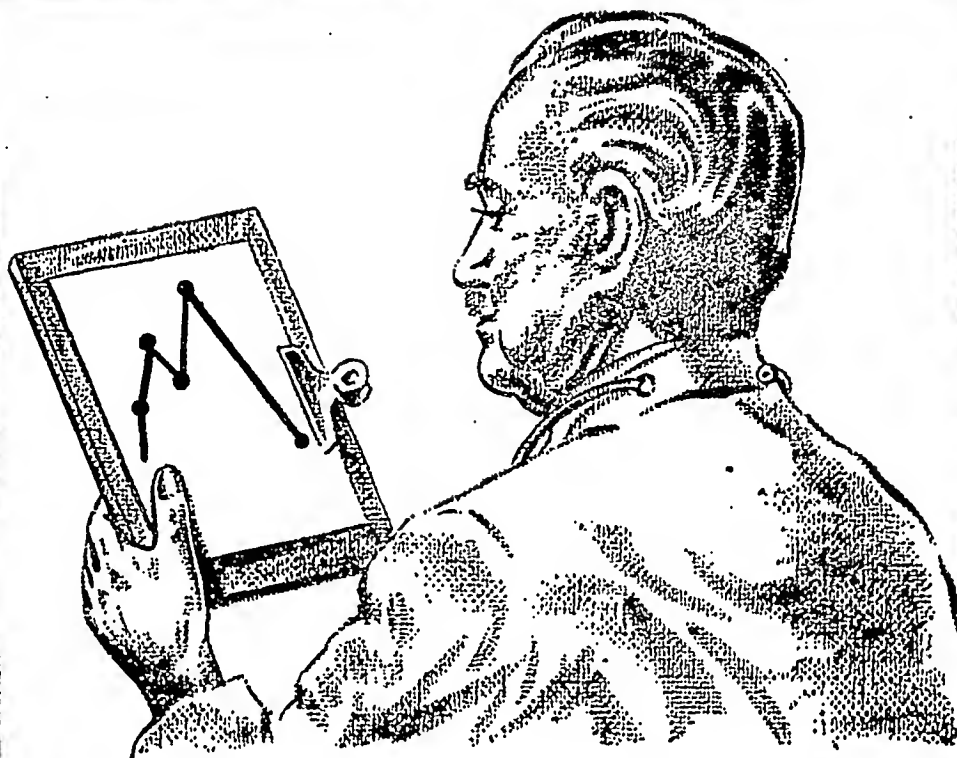
The clinical features of the case with positive W. R. coupled with the response to anti-syphilitic treatment leave no doubt that the case was one of syphilis of the stomach.

### Acknowledgment

My thanks are due to Major-General H. C. Buckley, M.D., F.R.C.S., C.S.I., I.M.S., Principal, Medical College, and Superintendent, Thomason Hospital, Agra, for his kind permission to publish the report of this case.

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# Indian Medical Gazette

DECEMBER

## THE LABORATORY IN MEDICAL PRACTICE

IN recent years, laboratory tests applicable in numerous diseases have rapidly increased, and nowadays the physician, particularly in hospitals with adequate laboratory services, receives great help in the diagnosis of many diseases from the laboratory. This is an excellent thing for which all clinicians are grateful. But these gains have been partly offset by certain losses, and in certain spheres of medicine, particularly tropical medicine, the development of laboratory aids to diagnosis has had bad effects. We will discuss some of these bad effects.

The first is a neglect of clinical examination. As students we were all told that mistakes in diagnosis are usually due not to lack of knowledge but to lack of adequate examination of the patient. The importance of thorough and careful history-taking and of complete clinical examination of the patient from head to foot, system by system, is constantly impressed upon us. How little some of us carry this into practice! We find laboratory tests so commonly used that we tend, particularly in tropical diseases, to feel that the diagnosis of the case is likely to depend upon laboratory or other non-bedside findings, and our clinical examination tends to become more and more perfunctory to the detriment of our patient, ourselves and our work.

Secondly, we all tend to an undue dependence upon laboratory findings. Most practitioners of medicine particularly in India have to attempt to diagnose and treat most of their patients without the aid of laboratory findings, and even those of us who normally practise in hospitals with laboratory facilities may at any time find ourselves called upon to make a diagnosis in serious illness without any laboratory to help us. It is in these circumstances that the weakness of our clinical medicine becomes apparent.

In medical teaching institutions in this country, laboratory facilities are usually available and are fully used; many teachers however tend to forget that most of the students under tuition will have to practise with little or no laboratory facilities. With the present-day neglect of clinical medicine, students are getting the idea that, without laboratory facilities, accurate diagnosis is difficult or impossible. This idea is a most unfortunate one. Many diseases, even tropical diseases, can be accurately diagnosed by a proper application of ordinary methods of clinical examination. It is of course

very desirable that laboratory confirmation of diagnosis should if possible be obtained, but we should all have sufficient knowledge of ordinary clinical medicine, and sufficient faith in our own clinical judgment, to make a firm clinical diagnosis in the majority of cases which we encounter.

The laboratory, instead of being our servant, helping us in diagnosis, either confirming or else sometimes throwing doubt on our clinical diagnosis, tends to become our master. The physician, instead of being the master of the situation, the careful examiner, the accurate recorder of clinical findings, the careful interpreter of laboratory findings and by these methods arriving at a diagnosis, tends to become the mere acceptor of laboratory findings and sometimes the slave of the laboratory. This is all wrong.

In medical literature in these days the term 'laboratory diagnosis' is often used. A more misleading term could hardly be thought of. Diagnosis is a mental process, undertaken by the physician carefully weighing all the evidence and arriving at conclusions. Laboratory findings are valuable, but they are only part of the evidence to be considered by the physician. There should be no such thing as laboratory diagnosis. It is true that even experienced physicians practising clinical medicine without laboratory aid may make mistakes; but we should remember that the laboratory also is by no means infallible.

It is good that we should think of the many ways in which the laboratory can and sometimes does lead us astray.

In these days when malaria is so common and many people are harbouring malaria parasites in their blood, many of us are meeting cases in which a patient is suffering from some other infection, and the finding of a few malaria parasites in the blood does not necessarily indicate the cause of the illness. Recently we recorded in this journal a case of cerebrospinal meningitis in which the finding of *P. falciparum* in the blood was made but was not allowed to overrule one's clinical judgment that the case was not one of cerebral malaria. Numerous such cases have been encountered recently. The finding of typhoid antibodies in the blood in a titre which would normally be diagnostic is, particularly in these days of widespread inoculation, not always an indication that the patient's fever is due to typhoid. Moreover the frequency with which the titre of antibodies in the blood rises during an attack of fever due to a completely different cause (e.g. an 'anamnesic' reaction) is being increasingly realized. The recognized causes of a false positive Wassermann are constantly multiplying. Even the Weil-Felix reaction is now reported sometimes to give positive results in pregnancy. Many other examples could be quoted in which laboratory findings have to be interpreted in the light of clinical findings, and

even sometimes have to be ignored in diagnosis. Recently we examined a patient in whom the clinical evidence of syphilis was overwhelming but the doctor had not made the diagnosis because the Wassermann reaction happened to have been reported negative. In such circumstances laboratory evidence may have to be ignored. The same is true of x-ray findings. Within the last year we have seen several cases in which tubercular infiltration of the lungs has been reported by experienced radiologists, and yet the clinical evidence was against this diagnosis, and the clinical diagnosis proved to be the correct one. Not that the writer would minimize the value of x-ray in the diagnosis of lung tuberculosis, because x-ray evidence is generally the most reliable of all, but nevertheless it is not infallible.

Since drafting the above, the editor has seen several references to the same subject in other medical publications. In a book recently published, the writer, W. C. Alvarez, discussing the modern reliance on laboratory methods in diagnosis made the following remark:—

'Recently out of 50 candidates asked the simplest way to distinguish between obstructive and non-obstructive jaundice, only three said they would look at the stools; all the others said they would have a van den Bergh test done. A test of doubtful validity as opposed to a simple conclusive observation. Candidates often refuse to diagnose a straightforward case of aortic regurgitation without a Wassermann reaction, and will ask for an electrocardiogram without feeling the pulse. When directed to do so it seems to convey no information to them. One could multiply examples.'

In a recent article on medical education the following sentence appears:—

'The emphasis being laid on observation, the student would learn to see laboratory methods in their proper perspective, as aids to bedside diagnosis; and whenever a laboratory test disproved a clinical observation which he had made, he should not rest until he had discovered whether, and if so how, his senses had led him astray.'

We would support this statement, but would go even further and say that no laboratory test can 'disprove a clinical observation'. It can only give evidence for or against a particular interpretation of a clinical finding.

It appears that the medical profession is realizing that undue dependence on laboratory methods in diagnosis is very common among medical men to-day, and that we are losing our ability to observe accurately, to examine carefully and thoroughly, and to interpret wisely our clinical findings. These are the most important attributes of the good physician, but we tend to let them atrophy from disuse.

It would be good if all practising physicians could keep at hand and read through periodically, not less than once a year, a good book on clinical methods practicable at the patient's bedside, and if they used these methods whenever possible. It is good practice, whenever a new patient comes for examination, to make a complete clinical examination before ordering any laboratory tests, or before study-

ing the laboratory reports already available. Of course there are exceptions. It would be foolish in an emergency such as that presented by a probable or possible case of cerebral malaria to spend an hour on clinical examination before having a blood film examined. Every case has to be judged on its merits, but the time spent in thorough examination of patients is never wasted. Every now and then in routine examination one comes across a completely unexpected finding which immediately makes accurate diagnosis possible. This is where the good clinician will score heavily. More often, however, it is not one unexpected finding of major importance but the detection of a number of minor points which, when carefully considered together, point clearly at the true diagnosis. This is an even better test of a good clinician.

If these things are ignored or neglected, and if we depend largely or entirely on the laboratory, more than half the fun of being a physician disappears, and our profession instead of being the thing for which and by which we live, and providing an unending source of interest, becomes more and more mechanical and may become a drudgery. Moreover our patients will suffer. They are human beings suffering from various ailments and they come to us for relief. Our patients must remain our prime interest, and this interest must not be stifled under a mass of laboratory reports. Laboratory and other aids to diagnosis are very great assets, but they should be kept in their proper place as the servants of the clinician and not allowed to become his masters.

J. L.

## MEDICAL SCIENCE IN INDIA

WE would draw the attention of our readers to the special article printed in our present number on the present position of medical science in India by Lieut.-Colonel G. R. McRobert. The author of this article has obviously in the past and is now giving much thought to the future of medical services and of the medical profession in this country, and in a recent number of our journal published an article on 'Indian degrees for Indian graduates' which has been very widely and very favourably commented on in many quarters. The present article discusses another matter of great importance in an equally able manner.

Colonel McRobert states that 'The overseas man of science coming to India to-day is astounded to find that we have in this land rival systems of medicine'. The editor remembers soon after his arrival in India many years ago being questioned by Indian friends regarding the nature of the medicine that he practised. I did not know then of the cults of medicine in this country, ayurvedic, unani and other

indigenous systems, not to speak of homœopathy and other such fads. I was asked whether I practised allopathic medicine, a term which I had never heard previously and did not know the meaning of. My reply was that I tried to practise scientific medicine, and I objected to terms such as western medicine and allopathic medicine, for scientific medicine is international and is not confined by geographic or any other boundaries. As Colonel McRobert states, science is one and indivisible and international. There was a time when in India medicine was probably as much or more advanced than in any country in the world. Indian medicine markedly influenced Chinese medicine, Arabic medicine, and, through the Arabians, European medicine, for even then medicine was already international. To try to introduce nationalism into science is a retrograde step.

We would support Colonel McRobert's appeal, 'Let India march in step with other nations in the conquest of disease and suffering and not sigh overmuch on long past glories of the Vedic times'.

It must be said that in discussing these matters in the *Indian Medical Gazette* we are preaching to those already converted, for the readers of our journal will already share these views. This may be so, but nevertheless we as medical men are constantly finding ourselves involved in discussions with laymen on these subjects in private or in public, and the ability to state our case clearly but sympathetically against opposition may be very useful to us; in this matter we can all learn much from Colonel McRobert's article, for it is obviously the result of much thought and his views are clearly stated and presented in a way which few could hope to equal.

J. L.

## Special Articles

### THE POSITION OF MEDICAL SCIENCE IN INDIA

By GEORGE R. McROBERT, C.I.E., M.D., F.R.C.P.  
LIEUTENANT-COLONEL, I.M.S.

*Professor of Medicine, Madras Medical College,  
Physician, Madras General Hospital*

IN an address entitled 'William Harvey's message to India' delivered in 1928—the tercentenary year of the publication of William Harvey's masterpiece 'De Motu Cordis'—I drew the attention of a medical audience to the urgent need in India for a more realistic, objective and scientific outlook on problems relating to Medicine. I (1929) alluded to the danger of allowing pseudo-patriotism, obscurantism and superstitious ignorance to stand in the way

of progress. To-day it is more than ever necessary to reiterate such a warning.

We are in the midst of great change, political, social and economic. In all probability new developments in these spheres will be more marked in India than in any other part of the world.

The great Indian textile firms, the producers of steel, the heavy chemical industry, locomotive and aeroplane manufacturers, shipbuilders, potters and electrical engineers are all planning to harness the latest advances in science in aid of their ventures.

The ancient craftsmen of Mohinjadara, the wise men of Taxila and the venerable scholars of Pataliputra receive their respectful due in works on Indian history and anthropology, but they and their ideas will not be permitted to hinder the progress of the industrial technocracy who are eagerly pressing forward their schemes for a modernized India.

Can the same be said of the science most urgently needed in India to-day—the science of medicine, the science of producing and guiding and comforting the human race in health, of aiding it in time of sickness and sometimes of even curing its diseases?

The answer is a very definite 'No'.

All up and down the land a steady agitation goes on for the official recognition and encouragement of 'Indian National medicine' with Tibbi.

Governments of provinces and of Indian States alike donate moneys from the public purse for the propagation of such hoary systems and for the erection of colleges, schools and hospitals for their spread.

This is a most astonishing state of affairs. Scientific medicine has been taught in India for over a hundred years in our medical colleges and schools. It is most disconcerting to find that at this late date not only are the hundreds of millions of the ignorant peasant population 'pathetically contented' with 'indigenous systems' but that a high proportion of the educated classes are of like mind.

The position of the members of the legal profession as leaders of the people in political, social and educational spheres is so outstanding that it is worth while to find out the views of that influential and important body of men.

I have a number of Indian friends and acquaintances on the bench of the High Courts of judicature and among senior Indian counsel; during the past few years I have had under my care in hospital and elsewhere many political leaders and other intellectuals—mostly drawn from the ranks of the law. I have been disappointed to find that nearly all have a strong predilection for the indigenous systems.

Discussion reveals three main reasons for this curious preference:—

(a) A complete lack of knowledge of the foundation upon which scientific medicine is being built up.



(b) Ignorance of what scientific medicine has achieved and of the rapid advances now being made.

(c) A feeling that, although indigenous systems may not be very efficient, they are cheap to apply and to administer, and that scientific medicine is too costly for the country to afford.

It may be worth while to examine these three points.

The science of medicine is a very ancient one. It progressed slowly throughout the earlier ages of history—such slow advance as there was being arrested from time to time by religious prejudice or by undue reverence for alleged authority. In the early seventeenth century a great step forward was made when William Harvey put experimental investigation into problems of physiology on a sound basis; but it was not until the middle of the nineteenth century that medical science became firmly established on a secure foundation. The invention of the compound microscope, the rapid development of organic chemistry and, latterly, of biochemistry and biophysics have led to such amazing advances that we can say with truth that 95 per cent of the total corpus of knowledge with regard to the working of the human body has been obtained within the lifetime of men who are still with us such as Sir Thomas Barlow, an ex-President of the Royal College of Physicians.

We are still groping towards the light, we are extremely ignorant *but we know it*, and sometimes it seems that the more that is revealed to us the less we understand of the ultimate meaning and purpose of it all.

The greatest advances have been made by men tackling problems concerned with the fundamental principles on which the living cell works and continues its existence—the nutrition and excretion of the simple cell, its modes of reproduction and responses to stimuli. Aggregations of cells forming simple tissues are examined from all scientific angles, in order that information may be obtained of the way in which different environments and stimuli may affect the more complicated collections of cells and tissues forming organs and complete animals. Research into fundamentals is what eventually brings the richest of all rewards—an understanding of the primary laws of nature—for without that, no real progress can be made.

It may surprise some to know that nearly all advances in the science of medicine now come from men who have nothing to do with medical practice or with the care of the sick but who have a special knowledge of and training in the fundamental sciences of physics, chemistry and physiology.

In the British Empire one 'honour' far transcends all others as an indication of outstanding meritorious work in Arts, Science or Statesmanship—the Order of Merit (O. M.). At the present time four British medical men hold this coveted distinction—Sir Charles Sherrington,

Sir Gowland Hopkins, Sir Henry Dale and Prof. E. D. Adrian. Not one of these has ever practised medicine or had dealings with patients. All are physiologists investigating, in the laboratory, the fundamental properties of living matter.

We cannot proceed very far with investigations into the changes produced in the body by disease if we do not have a thorough understanding of the mechanism of the healthy organism. So it is that these workers on the principles of the integration of the nervous system; the fundamentals of nutrition; the relationship between nervous impulses and the release of chemical activating agents; and the electrical changes which take place in the brain during cerebral activity are awarded the highest possible honour by the King.

The day is fast approaching when it is unlikely that such advances will be made by men holding 'medical qualifications' of any sort, as the increasing complexity of problems in biochemistry and biophysics demands such rigorous training in the methods of these sciences that years spent in gaining bed-side experience in elementary midwifery and surgery are really wasted. The layman sometimes finds it difficult to grasp the fact that scientific workers on problems connected with the human body need not be medical men or 'doctors'; that a research biochemist may at one moment be tackling a problem concerning the hormone content of the thyroid gland, at another the constitution of a coal-tar dye and at yet another, the germination of wheat.

Science is one and indivisible. No advance is possible in one subdivision of knowledge without its reflection in all other subdivisions, and rejoicing over a discovery is not to be confined to the members of the particular scientific band immediately concerned.

It is a lack of appreciation of these elementary facts that is at the root of our trouble in getting scientific medicine accepted by the leaders of India to-day.

Their education is defective so far as leading them into contact with problems of science as it affects everyday life is concerned.

Literature, the classics, moral and mental philosophy afford fine training for the mind, but however good such training may be, it does not give the slightest inkling of the marvellous fields of exploration which form the life's work of so many scientific men of importance in the world to-day.

I have tried to persuade more than one outstanding political leader to read Hogben's and Crowther's semi-popular works on the meanings and methods of science, but with complete lack of success.

The overseas man of science coming to India to-day is astounded to find that we have in this land rival systems of medicine.

I feel that the acquiescence of our intelligentsia with this extraordinary state of affairs

is due to a false analogy drawn, consciously or unconsciously, between medicine and the law.

Now the word 'law' has two chief meanings. Law (man-made): eustomary rules recognized by a community as binding; law (natural): a correct statement of invariable sequence between specified conditions and one specified phenomenon.

The lawyer is concerned with man-made laws: the doctor with natural laws, and they have no connection with one another.

In India, Muslims, Hindus and Christians so far as property, inheritance and certain social relationships are concerned are subject to entirely different systems of law—rules for the conduct of affairs in different communities fixed in accordance with ancient tribal customs or codes.

It is not unnatural that people accustomed to the idea of control of society by several entirely different systems of law should take kindly to the notion that nature's laws are likewise arranged differently for different religions and castes.

The laws of nature, however, do not vary with tribe or race, with country or continent, planet or universe.

In Cape Town and Oslo, sulphuric acid has the same action upon zinc, iron is iron on our own Sun and on Sirius, the leg muscles of the Derby winner are activated by the same chemical substance as is liberated by the nerve endings in the wing muscles of the humming bird.

In the course of an abdominal operation, it is impossible to tell whether one is dealing with the viscera of one of Aryan, Dravidian, Mongolian, or Ethiopian stock.

The bodies of all are constructed on the same lines and obey the same laws of nature.

The suggestion that the body of the Muslim responds best to treatment by the Unani system, whereas disease attacks the Hindu according to the pathological processes recorded as the inspired guesses of the sages of the Vedic period will not bear examination.

I have elsewhere pointed out (1929) that although, as the years go by, we are becoming more and more able to appreciate the mysterious processes of nature and to probe some of her manifold secret places, we freely confess our ignorance on many points.

It is this willingness to confess ignorance, to re-open and re-examine in the light of fresh experience and new evidence theories however apparently secure and generally accepted, and to test fully any suggestion based on sound evidence that marks out scientific medicine from the old traditional systems.

Nevertheless, we are constantly faced on the platform and in the press with demands for the teaching of 'National Indian medicine'—whatever that may mean.

Turning now to the past, present and future achievements of scientific medicine, let us look at these mainly as they affect India.

A high proportion of the diseases which affect mankind especially in the tropics are caused by parasitic invaders belonging to the animal or vegetable kingdoms.

Some of these like many of the parasitic worms, hookworm, round worm, guinea worm and blood worm (schistosome), are visible to the naked eye. Others can be seen by the human eye only when magnified by a lens or microscope.

A third variety are so small that they cannot be seen by the aid of even the most powerful microscope, though we now have means of demonstrating them by recently produced electronic scientific devices. These exceedingly minute organisms are the ultramicroscopic viruses. They have as yet failed to respond to any drug treatment.

The disease-producing organisms of the larger kinds—the worms or helminths, the microscopic bacteria and the unicellular protozoa—have been succumbing with almost breath-taking rapidity before the onslaughts of scientific researchers in pharmacology.

Excluding the viruses, we have now powerful chemical weapons at our disposal to act on nearly every known harmful parasite with the exception of two bacilli—closely related cousins—the tubercle bacillus and leprosy bacillus which have been provided by nature with an acid- and drug-proof armour-plating but we can confidently hope that these two bacteriological panzers will soon fall to an as-yet-undevise'd chemotherapeutic rocket. Not only are the number and power of these synthetic drugs increasing rapidly, but a further important development has recently taken place. We are now gaining some idea of exactly how these new drugs produce their beneficial effects.

Until not long ago we had to be content with the knowledge that a particular chemical compound had lethal action on a certain noxious micro-organism.

When sulphanilamide was introduced, we knew that its presence in the blood-stream reduced or abolished the number of streptococci causing septicæmia. Now we believe we know exactly how it produces its beneficial effects, and organic chemists have accordingly worked out a bewildering number of derivatives of the original sulphanilamide each less toxic and more potent than the last.

We have as yet little means for dealing with virus diseases after their onset, but science has provided in vaccination with modified strains of disease-producing viruses a degree of protection against attack by such diseases as smallpox, yellow fever and rabies.

A few words may be said about the replacement of ductless glands which have failed in their purpose by extracts of similar glands from animal bodies.

Myxœdema, Addison's disease, pernicious anæmia and diabetes mellitus are typical

examples of formerly fatal diseases which have recently been efficiently countered by replacement therapy, using extracts of glands from animal bodies. Here again, the organic chemist has stepped in, providing synthetic substitutes for hormones naturally produced in the glands of living animals.

In addition to the misery caused in India by actual deficiency in the quantity of food—in its capacity as a fuel or energy producer—an almost incalculable amount of harm is done in this land by the poor quality of food which in many districts lacks essential salts or vitamins.

In this respect insufficient tribute has been paid to Sir Robert McCarrison who deserves very well of India not so much for any single piece of research in the science of nutrition as for his early recognition of the vast importance of modern methods of nutritional research to the welfare of the people of India, for his loud and clamant propaganda for improvement of our national dietaries, and for the foundation of the model institute which is now attacking important problems of nutrition from all angles.

The amount of genuine advance in our knowledge of food-deficiency diseases is astonishing.

You must not believe everything you read about vitamins in the advertisements of the manufacturing chemists, but the fact remains that research workers on nutritional problems have of recent years given us a very much clearer idea of what we can and should aid at in framing diet schemes for the people.

In a final reference to the achievements of scientific medicine, I may mention malignant disease or cancer—a condition in which for some unknown reason certain cells of the body multiply in an abnormal fashion according to no known rules, separate off from their proper places and wander hither and thither in the blood or lymph stream, settling down here and there throughout the body as secondary growing malignant tumours.

Cancer has always been the supreme medical puzzle.

Recently it has been shown that one of the most fatal and painful of human cancers—cancer of the prostate gland—responds well to treatment by injections of extract of the female ovary. Not only so, but an artificial synthetic imitation of this ovarian extract, readily manufactured, will act equally well.

What a vista this opens out!

Are the organic chemists about to present us with synthetic hormonal-chemical remedies for cancer? It seems not unlikely.

I think I have said enough to show that scientific medicine is at the same time humble, progressive and increasingly successful and efficient.

I must now deal with the third reason advanced for encouragement of Ayurvedic and other indigenous systems.

It results from a confusion of ideas and a lack of knowledge of the difference between 'indigenous medicine' and 'indigenous medicines'.

**Indigenous medicine**—A corpus of knowledge concerning the maintenance of health and the treatment of disease handed down as tradition from Vedic times.

**Indigenous medicines**—Drugs naturally occurring in this country.

I recently read of a minister of an Indian State who in opening a school for instruction in a system of indigenous medicine stated that indigenous medicines were everywhere at hand whereas 'Western medicine' needed to import expensive drugs.

Every important and therapeutically active drug could be and in my opinion should be mass produced in India and thereby become an indigenous drug. There is no reason why, after the war, the best organic arsenicals, antimonials, sulphonamides, etc., should not be produced in India on such a large scale that the prices will come tumbling down.

Even when former foreign plants are used as a source of drugs, as in the cases of South American cinchona, Russian santonin, Austrian digitalis and Australian eucalyptus, suitable soil and climate for cultivation can be found in nearly every case in some part of India.

Scientific medicine has never been parochial in its outlook. In the old days, the sailing ships of merchant adventurers roamed the whole world over in search of spices for preserving and flavouring food and for herbs, roots and barks for the distillation or extraction of substances of medicinal value. India furnished its quota of these to Europe.

As time went on, it became evident that the inventive power of man had placed in the hands of organic chemists of all lands means of synthesizing or piecing together chemical molecules with powerful actions on certain diseases.

Nevertheless a world-wide search goes on by botanists and pharmacologists into the plant life of all parts of the globe for at present unrecognized substances of medicinal value.

For a good many years now the game has hardly been worth the candle—although an occasional find of some importance results as in the case of ephedrine from the Chinese plant—Ma Huang—but it would probably be better now to spend the time and money in building up new synthetics; *but the search does go on* and so far as India is concerned an active and systematic investigation has been proceeding for many years by trained pharmacologists into the therapeutic possibilities of Indian plants—with disappointing results.

Englishman and Japanese, German and Chinese, American and Arab, Indian and Pole all play their part—at any rate in times of peace—in a concerted drive against disease and in the study of organic chemistry and pharmacology, building up atom by atom, and molecule by molecule, weapons with an astounding capacity to deal with disease.

How can this be called 'Western Medical Science'? 'International scientific medicine'?

is the only permissible term. 'Indigenous system of medicine' does not mean a science which employs indigenous *medicines*. That is perhaps an economic ideal which may not be difficult to attain. It means systems of medicine practised according to the ideas of hoary sages of pre-scientific Vedic times, using only the means and methods known to the ancients with all their deficiencies and drawbacks.

That is a very different thing.

By all means investigate any points of apparent value in these systems, and if suitable incorporate the facts into the general body of scientific knowledge.

The place of Ayurveda is an honourable one—in the history of medicine and anthropology.

When naming new wards in modern hospitals, I should delight to see the names of Susruta, Charaka and other ancient sages inscribed as a reminder of those who have worked in the past and achieved a measure of success in their time, but so far as the future is concerned, I should say 'let India march in step with other nations in the conquest of disease and suffering and not sigh overmuch on long past glories of the Vedic times'.

I regret that the argument has been used that governments can afford to palm off inefficient and cheap indigenous systems of medicine, using unstandardized and unknown nostrums, on village folk because these poor people do not know any better and are quite content with it.

We have been told that the replacement of traditional systems of medicine by modern medicine may be logically right but it is psychologically wrong.

It may be that, so long as practitioners of indigenous systems pay lip service to their creeds but actually use quinine, emetine, sulphonamides and mapharside in their practices, less harm than might accrue actually does so; but that in my opinion is a remarkably poor excuse for the further propagation of systems which cannot hope to compete honestly with international scientific methods.

My main thesis is that we need to educate the Indian public, well-to-do and poor alike, in the mode of working of the human body—elementary physiology and the rudiments of hygiene—and that with better science education and with an increased knowledge of the aims and methods of preventive medicine, the demand for the spread of the benefits of our science to the uttermost parts of the land will become insistent.

I have dealt largely with the great strides medical science has made in the treatment of disease by means of therapeutic substances, natural and synthetic, but quite as important as that is the advance our science has made in the prevention of disease.

Prophylactic vaccination and inoculation, the provision of protected water supplies and of adequate milk supplies, and the control of noxious insects have all been shown to have

enormous effects on the rates of mortality and morbidity.

The fullest benefits from scientific medicine in the prevention and treatment of disease cannot be obtained till at any rate that educated portion of the populace who are responsible for framing policy and for its execution are fully convinced that the benefits which are obtainable from the science of medicine in all its branches are at least equal to those obtainable from modern chemical, engineering, electrical and agricultural practice.

Towards the end of their careers as doctors in this country, many look somewhat wistfully at the great dams at Sukkur and Mettur, at the fine flowing canals in what was at one time waste land, at hydro-electric systems and at intricate networks of rail communications, as solid and tangible evidence of the benefits conferred on the country by the modern engineer, and feel that their own contributions to India's good have been poor and ephemeral.

Careful reflection will however reveal that medical science, though less showy and easily demonstrable, has conferred at least equally important benefits on the land by pointing the way to a longer and healthier life for India's teeming millions, and the future is a rosy one if what the late Lord Moynihan would have called 'the hominal engineer' gets his due share of recognition as a nation builder and a real place in the direction of the country's affairs.

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### SERUM TRANSFUSIONS IN AIR-RAID CASUALTIES IN SOUTH-EAST BENGAL

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As surgeons in this country, we are so often working against odds loaded against us in the shape of anæmia, chronic malnutrition, chronic tropical diseases such as kala-azar and malaria, and sepsis, complicating our surgical cases. It is not to be wondered at, therefore, if our air-raid casualties were to show a heavy morbidity and mortality. And yet this has not always been the case.

What are the factors which will increase the chances of success for the wounded in raids or in battle? They are early, smooth, and speedy removal from the firing line; which includes the incident in an air raid, to hospital; efficient classification at hospital, pre-operative treatment, as early operation as is compatible with the condition of the patient; rapid but thorough operative technique, and skilful and careful post-operative care.

We are to-day concerned with that stage of the patient's progress when he has been admitted into hospital and is being got into a condition which will see him through his subsequent operation with every prospect of recovery which we can give him, and secondly with one aspect of the operation itself, and thirdly with the immediate post-operative period.

I shall speak only of the war casualty at first, and later show how my remarks can be adapted to peace-time surgery. By war casualty I mean primarily the air-raid casualty.

Wounds received in a raid are often of devastating severity—abdominal, with or without evisceration, perforating or penetrating injuries with internal hæmorrhage, or perforation of some hollow viscus, compound fractures, severe laceration of soft tissues, amputation by the missile, head injuries, abdominal and thoracic injuries and burns.

The importance of secondary wound or traumatic surgical shock has been given, deservedly, a high place in consideration of war wounds in the last war and in this. A brief résumé of the pathology and signs of surgical shock should be kept in mind. There is loss of fluid from the circulating blood, often by hæmorrhage, but not necessarily so, causing a lowered blood pressure, anoxæmia, loss of body heat, and sometimes death from heart failure, and failure of the vital centres of the brain. Clinical signs are coldness, a clammy sweat, lowered blood pressure, rapid low tension pulse, cyanosis, rapid respiration, with a terminal unconsciousness and œdema of the lungs; or else recovery with a rising blood pressure, improvement in pulse tension, recovery of normal body warmth. One is struck particularly with the coldness of the body accompanied by the poor pulse. With the experience of a few raids one comes to look for certain injuries which are not only common but also give the observer warning to expect severe secondary shock, and so forestall its onset partly or wholly. These are compound fractures, severe muscle laceration, partial or complete traumatic amputation, and abdominal and chest injuries. In Chittagong our most worrying cases were usually badly lacerated limbs; of these more anon.

What means have we for fighting shock, for it is a redoubtable enemy, and one which will claim a high rate of victims unless tackled with skill and promptitude coupled with surgical patience?

Mental and physical rest and quiet, reduction of pain and hæmorrhage by putting the patient quickly to bed with a full dose of morphia and by cutting out all unnecessary moving from stretcher to stretcher or bed to bed; warmth by blanketing, hot bottles and electric cradles, hot drinks, fluids; arrest of hæmorrhage, and immobilization of fractures; avoidance of all unnecessary disturbance such as changing dressings, changing clothing and clumsy physical examinations. Above all, premature operations

and anæsthetics are to be prohibited totally. This last factor is unfortunately lost sight of by many who seem to think that the height of surgical skill is immediate operation irrespective of the general condition of the patient. Nothing could be more unfortunate or fatal. Except for the arrest of severe arterial hæmorrhage, and the closure of an open pneumothorax, and a tracheotomy for impending asphyxia in connection with a neck wound, no case calls for immediate operation, not even abdominal wounds; these will always be improved, if improvement is at all possible, by an hour's resuscitation. Yet this is not a popular conception, as far as one can gather, amongst many of our doctors.

Our thoughts to-day centre on the vastly important weapon of fluid, and particularly on blood transfusion. I will not dwell on the various fluids which may be given intravenously but keep to whole blood and plasma or serum. Each of these has its place and indication. Transfusion of whole blood on a very large scale is not yet possible, and as far as we are concerned with raid casualties we are confined to serum.

There are two main pathological types which need transfusion—one where there has been a great loss of the fluid part of blood plus the cells—that is, hæmorrhage from various causes; the second where there is loss only of the fluid part of blood and a resulting concentration of the cells or hæmo-concentration. This is the condition—is surgical secondary shock pure and simple and is best typified by burns. One is led to believe that serum is certainly useful in cases of acute hæmorrhage where whole blood cannot be obtained for some reason or other. On the other hand it is unwise to give whole blood where there is no blood loss but hæmo-concentration, unless dilution of the circulating blood is first obtained by giving serum or glucose saline in sufficient quantities.

Now, how does all this apply to raid casualties? Take a typical example of a man admitted with a severe compound fracture of the right tibia and fibula with a good deal of tearing of the soft tissue into the bargain; quite a common occurrence. He has been wounded an hour or two before, and has had a dressing and some form of immobilization carried out by a first-aid party. He may have had other wounds. He is put into bed, and a brief note is made of his condition. He is probably cold and clammy, with a poor-tension rapid pulse, and a blood pressure of somewhere between 60 and 80 mm. systolic. His surgical treatment will be excision of the wound, alignment of the fracture, application of sulphonamide powder to the wound, a dressing of sterile vaseline, and a plaster of paris, all to be done under a full general anæsthetic. Can this be done safely at once? Certainly not, for he is in shock. First of all this has to be treated. If there is bleeding going on, more dressings and firm bandages are applied over his original dressing, morphia



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grain  $\frac{1}{2}$  having been given (presuming he is an adult), an electric cradle and blankets applied, and a serum transfusion started. He will be given one bottle fairly rapidly, in say 20 minutes, and his condition will be re-examined after half an hour. He may be still the same or may be slightly warmer; his pulse rather slower and blood pressure 90 perhaps. Another bottle is then indicated, and run into a vein, taking 40 minutes. He will then most likely have regained normal body warmth, a systolic of 100, a pulse of 110, and good volume. It is now safe for him to go into the theatre, but always be prepared to give him more serum during, or after, operation, although he will probably not require it. You will have many such cases as this in war surgery.

As far as transfusion is concerned you will find three clinical categories of patients:—

(a) The hopeful: those who respond rapidly and permanently with one or two bottles. Fortunately, these are a high percentage.

(b) The doubtful: those who do not respond, and whose chances are just touch and go. They sometimes need 4 to 5 bottles of serum to keep them alive over the first few hours; often they cannot be touched operatively for 2 to 3 days.

(c) The hopeless: these are frankly moribund—often a concealed abdominal hæmorrhage—who are definitely dying on admission, with multiple injuries, extensive burns, deep brain wounds.

Categories (b) and (c) are often difficult to distinguish and (c) patients are usually given resuscitation and perhaps a bottle of serum, but die shortly after coming in.

The unexpected often happens, especially with patients with burns who may pass rapidly from the hopeful to the hopeless. The doubtfuls in category (b) have proved, often enough, to be the most cheering and satisfactory cases, in that they are people dragged back from the brink of the grave. The great triumphs of serum transfusion here show themselves; firstly in preventing the hopeful slipping downwards into a lower category of doubtful or hopeless, and assisting the doubtful to final recovery.

From what I have seen in Chittagong, I am absolutely convinced that serum transfusion has saved dozens of lives, though it cannot work miracles. I have brief notes of 38 cases all wounded in raids in south-east Bengal. They all had serum transfusions, and were all very severe wounds or burns, many of them desperately bad. Of these 38, 15 were fatal either within a few hours, or later of pneumonia. That is a percentage of 31. The total mortality of all wounded, needless to say, is much less. These 38 cases had a total of 78 bottles of serum intravenously, an average of 2 each. Fifty-seven bottles were given prior to operation, 3 during an operation, and 18 after operation; 3 had rigors due to the serum, but 2 were without any real harm, as both recovered; the third died;

the cause of the serum reaction is unknown. No other untoward reactions were seen, and it is doubtful if the fatal case died by reason of the serum; the pulse rate on admission was 144.

It is of interest to enlarge on some of these cases to show you what type of case was given serum. By way of examples, I will instance 10 patients who recovered, and 8 who died.

### Recoveries

#### 1. J., aged 35.

Punctured wound below right eye; multiple lacerated wounds right thigh; lacerated wound left knee; lacerated wound left foot; multiple lacerated wounds forearm; multiple burns; pulseless on admission.

At 2-30 p.m. pulse 80, poor tension; 5-30 p.m. pulse 90, fair tension; 6-30 p.m. pulse ?, good tension. Five bottles serum before operation.

Operation next day.

#### 2. A. M., aged 27.

Lacerated wound right knee joint; compound fracture right tibia. Two bottles serum before operation. Recovered from shock within eight hours, and then operated on. Lost a lot of blood, and had one small whole blood transfusion on the fifth day. Progressed well.

#### 3. A. W., aged 26.

Lacerated wound left cheek; abrasion over elbow; lacerated wound right wrist joint; lacerated wound left knee; compound fracture right tibia. In severe shock on admission and recovered from this after 5 bottles of serum. Could not be operated on till third day. Still convalescing.

#### 4. J. A., aged 20.

Penetrating wound of abdomen with protrusion of viscera. Quite good condition on admission (at 2-30 a.m.) though cold, and probably on verge of shock. Blood pressure 110 systolic. Operated on at 5 a.m. Resection of 6 inches small gut which had been perforated in two places. Retroperitoneal space opened up by missile. One bottle serum given after operation. Had continuous gastric suction and intravenous saline drip. Good recovery.

#### 5. A. A., aged 25.

Incised scalp wound 6 inches long bone deep, comminuted depressed fracture right parietal bone, abrasion ankle. Moderate shock. One bottle serum before operation. Operation—excision of wound, removal and elevation of bone. Discharged at own risk after 25 days, perfectly fit, with wound healing cleanly and well.

#### 6. M. A., aged 40.

Badly shattered left forearm and arm with bone smashed as high as surgical neck of humerus. Moderate shock. One bottle serum before, one during and one after operation. Disarticulation at shoulder joint. Took a fair time, with limb difficult to control—stood operation well and made good recovery.

#### 7. M., aged 13.

Right leg blown off. Blood pressure before serum 50, after 85. Two bottles given before re-amputation. Recovered.

#### 8. M., aged 40.

Sucking wound of the chest with fracture of 2 ribs and great laceration of soft tissues. On admission semi-conscious. Temperature 97°F., pulse rate 120 feeble, respiration 50 shallow. One bottle serum. Blood pressure before transfusion 90 systolic, and after 122 systolic, and remained at 110 systolic thereafter. Discharged cured.

#### 9. Female, aged 25.

Four months' pregnant. Splinter wounds in back, arm, and hand; back wound was followed down to kidney which was not removed—presumably not badly damaged though I have no details. Hæmaturia plus plus. On admission rapid, feeble pulse, 140 per minute; respiration 40; blood pressure 86 mm.; collapsed during

operation but recovered after one bottle of serum when blood pressure went up to 124 and remained stable at 116 systolic. Discharged cured.

10. A. H., aged 12.

Lacerated wound right upper eyelid. Spleen plus plus on admission at 3-0 p.m. Pulse rate 160 and weak; shock severe. At 7-0 p.m. pulse came down to 134 and much better next day. Two bottles serum. Was a boy with enlarged spleen showing shock plus from a trivial injury. Discharged cured.

### Deaths

1. Unknown.

Abdomino-thoracic sucking wound of the chest with protrusion of mesentery. On admission:—Pulse rate 120; respiration 45; temperature 96.4°F.; blood pressure 76 mm. One bottle serum raised blood pressure to 90 mm. but patient died in a few hours.

2. Male, aged 30.

Badly lacerated wound of scrotum completely damaging testes and urethra; anus and sphincter destroyed and rectum damaged. On admission, pulse imperceptible; rapid shallow respiration. Temperature 96°F.; blood pressure 78 mm. One bottle serum raising blood pressure to 96 mm. Patient died in a few hours.

3. I., aged 32.

Penetrating wound right forearm; penetrating wound left forehead; gaping wound neck; shock plus plus. Pulse rate 144. Serum was started but patient had a rigor, and serum was stopped after  $\frac{1}{2}$  bottle. Died two days later of lung condition.

4. N., aged 18.

Severe compound fracture of left forearm with involvement of blood supply; penetrating wound back; lacerated wound forehead; severe shock. Blood pressure on admission 80 mm., half an hour after serum 90 mm. One and a half hours after serum 60 mm. Amputation of forearm and excision of other wounds. Died within 24 hours. This shows an attempt at rallying from shock, if the blood pressure is an indication, but was followed by a quick relapse. It also illustrates a difficult surgical problem as to whether to operate early in the hope that removal of the grossly damaged tissue may improve the general condition, or whether to wait. Three bottles of serum before operation, and 2 after, were given.

5. A. K., aged 12.

Head wound; severe shock. One bottle of serum was given, but patient died within the hour.

6. Male, aged 35.

Through and through injury of the right chest with hæmoptysis. On admission temperature 96°F.; pulse rate 115; respiration 45. Before two bottles of serum blood pressure 82 mm. and after 110 mm. Died of broncho-pneumonia.

7. Male, aged 46.

Compound fracture of right femur with much laceration of soft tissue. Patient clammy with imperceptible pulse; respiration 36 and shallow. Two bottles of serum, which raised blood pressure from 84 to 112 mm. but patient died within 24 hours.

8. Unknown.

Sucking wound of the chest with fracture of three ribs. Pulse rate 150; respiration 45; temperature 97°F. One bottle of serum, before operation. Blood pressure 92 before serum and 120 mm. afterwards. Died of pneumonia.

These cases quoted above are only a few of the total casualties sustained in south-east Bengal but serve to illustrate typical severe wounds caused mostly by anti-personnel bombs. Many cases were of a minor character; more were severe but either were not in shock or else had mild shock yielding to morphia and warmth.

When you consider that those who recovered, with the injuries just described, were poor-class peasants, coolies, and shop-keepers—none too

fit in normal times—you will agree that the human organism shows extraordinary vitality at times and that modern surgical technique does produce results; of the deaths one might be permitted to say 'No wonder they died with those wounds'.

In conclusion, I wish to thank Major John Brebner, M.B.E., Civil Surgeon, Chittagong, Dr. Dutta Gupta, Surgeon of our Comilla Mobile Surgical Team, and Dr. M. Das of Feni A.R.P. Emergency Hospital for their help in allowing me to use some of their case records. The patients quoted were operated on by Major Brebner and his staff, Drs. Gupta and Das and myself.

Above all we surgeons and patients alike must record our deep gratitude to Dr. Grant and his staff of the Blood Bank, and to the donors of blood. To him and to them, many owe their lives. We know what a powerful weapon for good the Calcutta Blood Bank has put into our hands. May their bottles never run dry!

## Medical News

### PENICILLIN

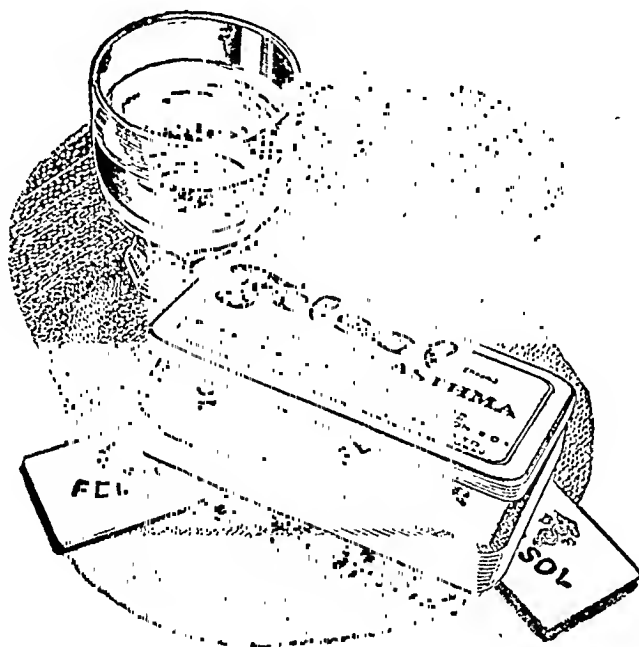
1. It is probably now a common knowledge that the American authorities have recently agreed to release limited quantities of penicillin for use of the civil population in India and as a corollary they have stipulated that all use of it must be under strict Government control.

2. In order to ensure that the available supplies are equitably distributed throughout this country and reach patients to whom its administration is justified in the current medical practice the distribution and use of penicillin is controlled by the Government of India through a committee consisting of five members with the Director-General, Indian Medical Service, as its chairman. This committee is known as the Central Penicillin Control Board and it is imperative now on every importer of penicillin to comply with any control rules and regulations that may be issued by the Board from time to time. Publication No. 1 of the Board has already been published. This besides giving the dosage and mode of administration of penicillin includes also the diseases in which penicillin is indicated and contra-indicated. Copies of this pamphlet have already been supplied to the heads of the Government Medical Departments in Provinces and States.

3. Naturally the unusual healing properties of penicillin have caught the imagination of the medical profession, so much so that often supply of this drug is requested for the treatment of indefinite cases where everything else has been tried and found to have had no results. One of the objects of the measures of control is to prevent this use of such a valuable drug. Its use is also prohibited in venereal diseases.

4. It is as necessary with penicillin as with sulphonamide, to know the nature of the infection to be treated. While some bacteria are extraordinarily susceptible to it, others are completely unaffected, and to use penicillin in an effort to eliminate them is a complete waste of valuable material. There are three groups of bacteria against which both the sulphonamides and penicillin are effective, with some important individual differences, and these account for most of the infections in which penicillin has been used.

5. Penicillin, in the first instance, will be supplied only to approved institutions, authorized to use this drug by or under the authority of the Board. Any stocks remaining over each month after the various Provinces have been allotted as much as they require will be sold by importers direct to medical practitioners



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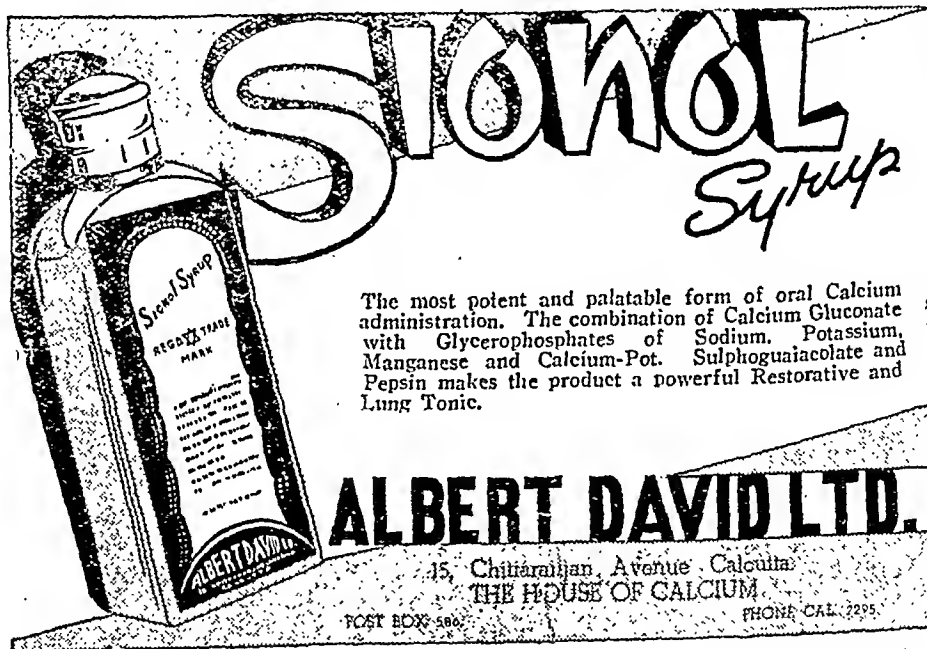
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and non-government institutions under the following control.

Every request for supply of penicillin in such cases must emanate from a medical practitioner and should be accompanied by a certificate that the case for which penicillin is required is suitable for treatment which should be signed by an Administrative Medical Officer, i.e. a Surgeon-General, Inspector-General of Civil Hospitals, Residency or Agency Surgeon, or any of the 'assessors' nominated by him for the purpose. These assessors will ordinarily be surgeons or specialists who have access to a suitable bacteriological laboratory.

In order to judge whether the use of penicillin is justified the 'assessors' will require particulars of the case which must include the diagnosis of the case, bacteriological findings, the doses, the mode in which penicillin is proposed to be administered and also the quantity required. If the assessors are satisfied they will sign a certificate that the case is suitable for penicillin treatment stating how much penicillin is to be issued. The importer on receipt of such a certificate will issue the amount of penicillin prescribed thereon. It is incumbent on every medical practitioner or institution obtaining penicillin to submit a case report through the Government Assessor on the prescribed Penicillin Chart copies of which have been distributed to Provincial and State medical authorities.

6. A considerable portion of the quota allotted to India has already reached the hands of the importers. Stocks of penicillin at present are available with Messrs. Kemp & Co., at Bombay, Madras, Calcutta and Delhi, Messrs. Parke, Davis & Co. at Bombay, Madras and Karachi, Messrs. T. M. Thakore & Co., Bombay, Messrs. Martin & Harris Ltd., Calcutta, Messrs. Volkart Brothers, Bombay, Messrs. D. M. Wadia & Co., Bombay, and Messrs. Smith Stanistreet & Co., Calcutta.

## XXI ALL-INDIA MEDICAL CONFERENCE, CAWNPORE

### ANNOUNCEMENT

The next Annual Conference of the Indian Medical Association will be held at Cawnpore on 26th, 27th, 28th and 29th December, 1944.

Members of the medical profession are requested to attend the Conference in as large number as possible in order to make the Conference a great success.

An exhibition of pharmaceutical products, surgical and medical instruments, etc., will also be held along with the Conference. Those interested in the exhibition of their products are requested to apply to the Exhibition Secretary of the Conference as early as possible.

A scientific section where papers will be read on medicine, surgery, ophthalmology, gynaecology, etc., will also be held. Scientists and members of the medical profession are requested to send papers for the same.

## BOMBAY MEDICAL UNION

The Bombay Medical Union invites theses from members of the medical profession for the following two medals:—

- (1) Dr. B. S. Shroff Memorial Gold Medal. The following subject has been selected for competitive thesis for 1944. 'Treatment of Burns—with special reference to the aetiological factors in shock as it occurs in burns.' The thesis must be in six clear typed copies.
- (2) Dr. Sir Bhalchandra Krishna Kt. Memorial Fund Gold Medal. Preference will be given to any original or research work especially with reference to indigenous medicine on western lines.

Each thesis should be designated by a motto instead of the writer's name and should be accompanied by a sealed cover containing the name and address of the writer and sent to the Hon. Secretaries, Blavatsky Lodge Building, French Bridge, Chowpaty, Bombay 7, by the 15th April, 1945.

## WILLIAM GIBSON RESEARCH SCHOLARSHIP FOR MEDICAL WOMEN

Miss Maud Margaret Gibson has placed in the hands of the Royal Society of Medicine a sum of money sufficient to provide a scholarship of the yearly value of £220, in memory of her father, the late Mr. William Gibson of Melbourne, Australia. The scholarship is awarded from time to time by the Society to qualified medical women who are subjects of the British Empire: and is tenable for a period of two years, but may in special circumstances be extended to a third year. The next award will be made in July 1945.

In choosing a scholar, the Society will be guided in its choice either by research work already done by her, or by research work which she contemplates. The scholar shall be free to travel at her own will for the purposes of the research she has undertaken.

There is no competitive examination, nor need a thesis or other work for publication or otherwise be submitted. The Society has power at any time to terminate the grant if it has reason to be dissatisfied with the work or conduct of the scholar.

Applications should be accompanied by a statement of professional training, degrees or diplomas, and of appointments together with a schedule of the proposed research. Applications must be accompanied by testimonials, one as to academic or professional status, and one as to general character. Envelopes containing applications, etc., should be marked on top left-hand corner 'William Gibson Research Scholarship' and should be addressed to Mr. G. R. Edwards, Secretary, Royal Society of Medicine, 1, Wimpole Street, London, W.1, and be received not later than 1st June, 1945.

## MENTAL DISEASES IN INDIA

At the request of the Medical Relief Advisory Committee under the Chairmanship of Sir Joseph Bore, Lieut.-Colonel M. Taylor, I.M.S., Medical Superintendent of the European Mental Hospital, Ranchi, has prepared a memorandum on this subject of which the following is a brief summary.

The attitude of the general public towards lunacy is still very crude and almost primitive, and the medical profession, for the lack of sound training, is inclined to look upon psychiatry as a kind of pathological curiosity. A propaganda programme to educate the public and cope with apathy and lack of understanding in the medical profession is the first essential. The Indian Lunacy Act, 1912, is out of date; it gives the impression that merely an alien is being dealt with, and not a sick man. It seems hard that before a case for mental disorder can qualify for treatment in a mental hospital, it must first have reached the stage of being certified. There is no provision for the diagnosis and treatment of recent and recoverable cases. In framing new legislation, the conception of a 'patient' rather than a lunatic must be kept in view. Attention must be directed to prevention rather than to cure. It is a very true paradox that insanity begins before a person is insane, and maladjustment ought to be treated early—and it can be treated early. The mental hospitals are so congested that there is hardly any room for voluntary boarders. The mixing of acute and recoverable cases with the chronic incurable is inevitable, and is thoroughly bad. There is no adequate medical staff. It is of the utmost urgency to associate with general hospital clinics where help could be given to the border-line cases without any feeling of stigma being attached to the treatment. The principal clinics would naturally be associated with medical schools, and there should be arrangement for both in and out-patients. There are hundreds of patients who would gladly avail themselves of this form of treatment. There is great need for convalescent houses and after-care associations for patients after the hospital care has ceased. The teaching of psychiatry to students in India is already inadequate, but no progress can be expected unless the colleges take cognizance of the great need for better psychological training. The trained social worker will be an indispensable adjunct in any scheme



of mental hygiene. Valuable space in hospital is taken up by many old people and chronic cases. They can be maintained at much less cost by establishing special houses.

No effort has so far been made in India to deal with the mental defectives. It is an immense and complicated problem, and some suggestions are put forward in the memorandum. Wholesale sterilization is outside the scope of practical politics, and is not worth consideration, but sterilization as an alternative to life-long segregation and with the consent of the defectives or their nearest relatives might be the most human course. Proper institutions will have to be provided, but it will be possible to house only part of the defective population in such institutions, and a large number will always remain outside under statutory supervision. Hostels and colonies can be utilized for those whose home environment is unsuitable. Occupation centres are now accepted as a most suitable adjunct to supervision. The establishment of special schools will also

form part of the scheme, and child guidance clinics must be associated with such schools. At first it will only be possible to deal with the type of defect which is easily recognizable, but the so-called border-line cases will in due course require attention.

#### THE ADA PRISCILLA HILL PRIZE

This prize (amounting to Rs. 150 approximately) will be awarded for the best essay on 'Social Medicine' entered by a student of the Lady Hardinge Medical College, or a graduate of the Lady Hardinge Medical College, within two years of graduation. Essays should be of about 5,000 to 7,500 words and should be addressed to the Principal, Lady Hardinge Medical College. Essays must be received before 31st March, 1945. A Committee of Examiners has been formed and the decision of this committee will be final.

## Current Topics

### Medical Education—A New Approach

(From the *Medical Press and Circular*, Vol. CCXI, 24th May, 1944, p. 321)

In an age in which the coinage of language has become so debased that the positive and superlative have become, for practical purposes, synonymous, almost any trivial event is likely to be described as epochal. Nevertheless that is the term which we as doctors must apply in its true, full and original sense to the Report on Medical Education recently issued by the Planning Committee of the Royal College of Physicians. This Report, from our professional point of view, is as important a document in its own way as the White Paper. Between them, should their main provisions be accepted and duly implemented, they promise largely to remodel our profession in the future—its status, its personnel, its aims and, more than probably, its achievements.

The Committee, which met under the chairmanship of Lord Noran on sixteen occasions, heard an exhaustive list of witnesses, either as individuals or as representatives of organized bodies, both lay and professional. Its recommendations therefore can scarcely be described as either hasty or ill-considered. That they may be described, in some degree, as revolutionary, shows to what extent our present system has lost touch with modern conditions and requirements—a revelation by the way that will come as no surprise to readers of our Educational numbers. Willy-nilly, it would seem, change, and quite drastic change as that, is inescapable.

The Committee first devotes its attention to the recruitment and selection of medical students at the present time. 'There are', the Report says bluntly, 'in our medical schools at present too many students who have neither the character nor the ability to make good doctors'. This would appear to be due primarily to the small numbers taking up medicine, which is itself a consequence of the expense entailed *vis-à-vis* the potential rewards. 'The doctor's way of life and his rewards must be made as attractive as possible if the standard of medical practitioners is to be preserved.' This is not to be gainsaid.

To remedy this, university education should, it is recommended, be made free. (It is nearly free as things are, since only about one-third of the cost of such education is recovered in students' fees.) Entrance to the university should not be secured by examination alone. 'This we should consider disastrous for several reasons. Firstly, securing a good place . . . would become the first aim of the schoolboy to the detriment of more important aspects of education. Secondly, a single examination is by no means a fair

test of ability. . . . Finally, no examination can adequately measure character and personality. . . . In the case of the doctor, character is in general not less important than ability'. Selection, it is suggested, should be made by 'a small body experienced in the assessment of character and ability, and acquainted with the requirements of medicine', and each selection should be reviewed at the end of the year. While this is a suggestion with which many will have considerable sympathy, it can be foreseen that it is one which might well arouse considerable opposition.

As for the curriculum in general, the Report, commenting on the chronic congestion and overloading that obtains, coupled with the incessant demand to take new cargo aboard, drily observes that 'a lay educationalist would scarcely be surprised to find that the product of so rigorous a system was often intellectually stunned'. Of the product—the average graduate, it notes: 'He tends to lack curiosity and initiative; his powers of observation are relatively undeveloped; his ability to arrange and interpret facts is poor; he lacks precision in the use of words. In short, his training . . . has been unsatisfactory as an education'. This it quite rightly attributes partly to the lack of co-ordinated teaching, but mainly to the tyranny of facts. It insists, and very right and gratifying we find its insistence, that what the teacher must impart is method; to swamp him in a sea of unrelated fact is merely to ensure his bewilderment, if not permanently to lame his mind.

But it is not alone the deluge of facts but the enormous and quite disproportionate importance assigned to memory that seems to us so mischievous. Memory is, of all the mental faculties, the most capricious and unpredictable, the least controllable and the least related to intelligence. Yet to the student, medicine might seem mainly an affair of memory. Not, be it noted, even associative memory, but memory for mere names, colourless and fortuitous patterns of sound. For our own part, our embarkation on the study of medicine was sensibly assisted by an examination during which we wrote essays, probably in highly questionable French, on Victor Hugo and Racine, and on Schiller and Heine in German of similar vintage. The change in intellectual climate a few months later, when we found ourselves committed to the arid desert of osteology, was almost stupefying; but it was merely a prelude to the imbecilities of topographical anatomy as we were taught it. That we subsequently won a scholarship in anatomy is less a matter for satisfaction than regret that so much time and effort should have been so largely wasted.

The Report does not mince its words. Early specialization at school should be discouraged, and



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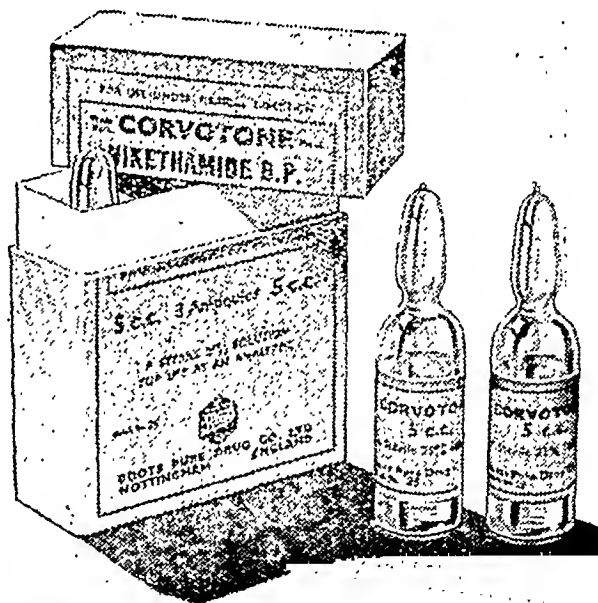
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the first M.B. should be taken at the university. Chemistry and physics should be largely confined to, and be illustrated by, their medical applications. Zoology should be curtailed to essentials, and 'botany be eliminated, apart from the physiology of green plants and bacteria'. In the pre-clinical years much of the detail at present required for the second M.B. should be omitted and anatomy taught as a living subject and not as a study of the dead. Physiology should be taught in relation to man rather than animals, and should be closely co-ordinated with anatomy and biochemistry. Whenever possible patients should be introduced to illustrate principles, and the methods of examining normal structures should be mastered at this stage. Elementary psychology in relation to physiology and pharmacology might well be introduced before the clinical period begins.

Last week we considered the Report on Medical Education made by the Planning Committee of the Royal College of Physicians, up to the point where the student is ready to embark at last on his clinical training in the wards. To-day we propose to resume our survey at that point and to follow him to his graduation, whence he shall embark on his career—provided these recommendations be adopted—very much better equipped to cope with his responsibilities than he has commonly been in the past.

In regard to the clinical, as to the pre-clinical curriculum, the Report is drastic if not indeed revolutionary. Its main proposal is that the whole framework shall be altered. Thus, instead of unleashing the new graduate on the public with his head crammed full of partially digested facts, in the keeping of a precarious memory, the Report proposes that the young graduate shall not be unloosed at all. After passing a first examination he will be entitled to practise, but only in hospital. Following a completed year in hospital practice he will then sit for his second 'final' after which, presuming the outcome to be satisfactory, he may practise where he will.

As for the examinations involved, they should not be nearly so formidable. For if the Report is at pains to emphasize anything, it emphasizes that clinical training must first and foremost teach *method* and *principle*, and give continuous scope and practice in the formation of judgment. The first of these 'finals' will test the candidate's theoretical knowledge of these methods and principles, and the second—the proof of the pudding, so to speak—will test his practical ability to apply them. The whole scheme in fact would operate to bring our procedure very much into line with the best American practice in the matter.

In regard to the details of training, nothing very unusual is propounded. But it is stressed that the first few months of clinical study should be carefully graduated to effect a smooth and easy transition from pre-clinical days, and that simple things should come first. Co-ordination of the clinical with the pre-clinical, and of one clinical division with another, so that the student is always building without interruption of continuity on what has gone before, is regarded, and rightly regarded, as the ideal. It is clear, of course, that to achieve this, much more forethought and hard work will be demanded of the teacher, if cases are to be presented 'not because they happen to occupy adjacent beds, but because they illustrate some pathological process', and much hospital etiquette will have to be discarded if access to all the clinical material available is to be at the student's and teacher's disposal.

In particular the Report lays stress on the adequate teaching of clinical methods by the specialists in question and on the student's familiarizing himself with the special departments (such as x-ray, etc.) by going along with the patient and carrying out some of the simpler tests and pathological investigations himself. Pathology and bacteriology are to be shorn of much of their non-essential detail, but their practical application cannot be too forcibly impressed. One type of clinical demonstration warmly recommended is the group consultation, where all the specialists concerned meet in front of the student and

discuss the case each from his own particular angle, and thus contribute each his fragment to the mosaic on which the final diagnosis is ultimately based.

Subjects to which more attention must be paid are psychology, social medicine, and especially pediatrics; adequately to teach the last, each teaching hospital should carry a unit of 60 to 100 children's beds. The Report, however, pronounces against separate examinations in these subjects. After graduation it is suggested that the House Officer should spend four months at General Medicine and four months at General Surgery, and the remainder either at Midwifery and Gynaecology, Pediatrics, or some speciality. For our part we confess that if the aim is to train primarily for General Practice, three months at each of the foregoing would seem a more logical allocation.

Where so much is excellent, one is tempted to look for more. Medicine, essentially one, is to-day so cut about and fragmented into specialities, obscuring those very principles to which the Report attaches such importance that one might have expected a bold attempt at a resynthesis for educational purposes. Thus the principles that govern infection are the same, whether exemplified in a boil, an infected wound, an osteomyelitis, an acute appendicitis, a tonsillitis, a bacterial endocarditis, a venereal or a notifiable, infectious disease, but these manifestations are so segregated and scattered that the practitioner, to say nothing of the student, too often fails to recognize their unity. To him they are so many diverse and separate entities, some of which—and more especially the notifiable infections—he tends to ignore, until practice reminds him sharply of his deficiencies, when he must learn by his mistakes.

Again, we note little emphasis on the study of health, or of its essential prerequisite, diet, although the public interest in this matter (which, again, is frequently extremely badly taught) has quickened enormously in recent years. The graduate may sometimes therefore experience the embarrassment of finding that his patient is better informed on the subject than himself. A dietetic department where the principles are expounded and research conducted, with its wards illustrating the deficiency diseases and the disorders of metabolism, is not commonly encountered, though it possesses undeniable educational advantages.

The Report, as it makes clear, is not concerned with methods of teaching, which in a way is a pity. Because it is our own conviction that unless the sound film is more and more widely substituted for formal lectures it will not be found possible adequately to teach the student even the revised and rational curriculum now proposed. Be that as it may, the Planning Committee deserves to be warmly congratulated. There is the first Report on the subject which we have seen that has faced the realities squarely, and made an honest and unprejudiced attempt to cope with them. We believe generally that their premises and conclusions are sound. If their recommendations be adopted, if the student of to-morrow, liberated from the tyranny of overwhelming facts, and from the appalling demands on his memory, is left free to apply his intelligence and develop his judgment, we believe that the standard of medical practice will rise considerably; a development that cannot fail to be reflected in a continually rising standard of national health.

### Training for Medicine

(From the *Medical Officer*, Vol. LXXI,  
4th March, 1944, p. 73)

Dr. F. M. R. Walshe, in 'Some Principles of Reform in Medical Education' (*British Medical Journal*, 5th February, 1944), roundly states those whose idea of reform is to add further to the overload of detail the student is expected to assimilate. Further, he pleads for severe pruning of what the student is required to know, or rather commit to memory, and for time to educate him to think, to observe, to deduce and to

evaluate the truth of the 'so-called facts, theories and conflicting opinions which make up the science and practice of medicine. There is nothing revolutionary in Dr. Walshe's proposals; Clifford Allbutt held much the same view fifty years ago when the mass of medicine was much smaller than it is to-day. Yet Allbutt saw that the appreciation of the theory of medicine was already being swamped by an overload of factual and fictitious detail. The object of undergraduate medical education should be to train young men and women in the principles which underlie the profession they are about to enter, to think in terms of health and sickness and understand the foundations on which all medical practice should be based.

The difficulties in the way of a sound training in medicine are formidable and Dr. Walshe does not belittle them. What is the theory of medicine? Can it be taught as a science, as a system built on untested generalizations? Can we deduce from the operation of appendectomy, or the use of sulphonamides in pneumonia, the general principles of deleting operations or chemotherapy? Is the science of medicine sufficiently far advanced that it can be taught as a science? We are slipshod in thought and in diction, but is not this because we have no guides which we can trust? 'It is surely impossible that we should forge generalizations and propound first principles until we have given precision to our language and thinking.' True without question, but how are we to gain precision?

At present the education of the medical student consists mainly in the assimilation of a vast number of unrelated facts and theories. He is not trained to evaluate the facts or to find the path of truth through conflicting theories. This omission must be ended and the only way this can be done is to teach medicine according to the principles of science. Unfortunately little of medicine is science in the sense indicated by a physicist or chemist; most of it is tradition, authority and empiricism and when submitted to scrutiny comes out so stripped that there is little left. Dr. Walshe's 'essentials of reform' are 'a carefully thought out pruning of the amount of factual knowledge we seek to impart, ruthlessly undertaken in order that the student may be enabled to develop a more thoughtful and critical attitude . . . and 'an explicit recognition of the necessity of a leaven of theoretical medicine, side by side with its vocational aspects. . . .'

We agree wholeheartedly with the pruning if we can find gardeners who know how to shape the tree to be fruitful, but to pursue the metaphor, injudicious pruning leads to a worse tangle of feeble twigs, and this has happened in medicine before now. Indeed all the specialists are eager to prune the stock in order to place their grafts and this is precisely what Dr. Walshe does not want. 'The provision of a category of teachers who shall develop it', the final essential of Dr. Walshe, is really the first, for without it we shall never get a start. But we believe that this is available or could be obtained if we entrust medical education to those members of the profession, who are able to teach and who recognize the teaching they give as important in itself. Professors do not necessarily know how to handle students, and specialists though they may be expert at their own job, are not always fit and proper persons to educate raw recruits in the fundamentals of medicine. Lord Moran, in his article 'The Student in Irons', quoted by Dr. Walshe, gave a very clear idea of the shortcomings of the present system and how it can be varied, for in the days when he was Dr. Charles Wilson he had very much to do with students, seeing some good and much bad teaching and what happened to those who received it.

What is taught to-day will be obsolete in a few years time. This is because what is taught and the way it is taught are faulty. Health and sickness are in essence always the same and an appreciation of what these really are will never be out of date. A thorough grounding in what can never be varied by fashion or increase in knowledge is the basis of technical education.

At the last attempt to reform medical education, in 1892 when the minimum length of the curriculum was increased from four to five years, the loaders and unloaders, to give them the least rude names by which they called each other, fought for the extra year. The loaders won, as was to be expected in the state of the theory of education 50 years ago. They would win to-day if what they wanted was possible; but it is not possible, for each of the thirty or more 'ologists who want to press their wares demand so much time that our short lives cannot accommodate them all, so they must be left to cut their own throats. The unloaders are united in their ideal and if they can frame a curriculum with comparable unanimity they must win. All the great leaders of medicine have been and still are unloaders. Between Walshe and Ryle of to-day and Allbutt and Osler of the past we can find no difference in principle and little in detail.

### Infective Hepatitis

(From the *Bulletin of Hygiene*, Vol. XVIII, May 1943, p. 428)

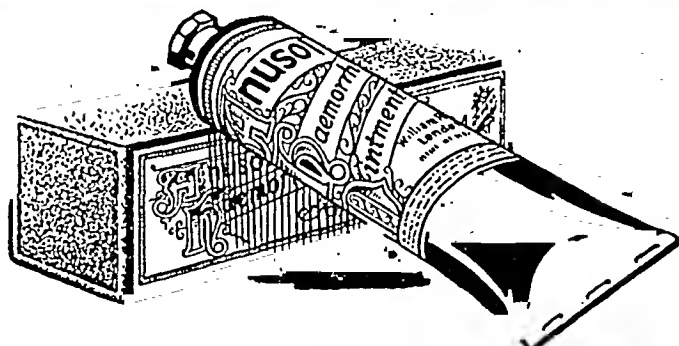
**Ætiology.**—The causative agent has not been identified, but the general opinion is that it is a virus. In spite of many attempts to infect animals with blood, bile, stomach washings and duodenal contents, none of the many animals tried has been found susceptible beyond doubt, though it is claimed in Denmark that the disease has been transmitted from man to pig and thence from pig to pig. This work has not been confirmed. Duodenal juice, blood and urine from patients with infectious jaundice have been proved infective for human volunteers. Nasopharyngeal washings were not tested in this experiment. Bacteriological investigation of blood and stomach contents has produced negative results only. Attempts to cultivate a virus on developing hen's eggs have not proved successful, though German workers have recently claimed that an infective agent has been carried through eight subcultures in fowl embryos, but it has been stated that the infective agent of the jaundice which has followed the injection of certain batches of yellow fever vaccine, or of convalescent measles serum, has been propagated in a medium consisting of chick embryo tissue, Tyrode solution and human or monkey serum. This agent will pass through bacteria-trapping filters, will withstand the action of weak phenol and may be frozen and dried and still retain infectivity. In these respects, therefore, it behaves as a virus.

'Confronted with such a baffling situation there is no alternative but to surmise that the reservoir of infection is man, among whom the disease is disseminated by droplet infection, and that the rapidity with which it spreads throughout a district is more compatible with a virus infection than any other group of pathogenic agent' (van Rooyen and Gordon, 1942).

**Epidemiology.**—Infectious jaundice has been reported from most parts of the world; the outbreaks usually occur in autumn and early winter. It has always been common in the bodies of troops; in the present war it has been seen in epidemic form in the German army in Norway and France and in British troops in the Middle East. Jaundice following the use of certain batches of yellow fever vaccine occurred at one time in the American forces, but since the use of serum, in the preparation of this vaccine, was suspended by the Americans, jaundice due to this cause has ceased to occur. Jaundice has also followed the use of measles and mumps convalescent serum, and a few cases have been reported after transfusion of pooled and dried human serum. From a large experience in the Middle East, van Rooyen and Gordon state that very few of their cases had received blood transfusion, and they conclude that, in respect of jaundice, the risks of transfusion are negligible.

Epidemics have often been reported in civil and military communities in which infection from vaccines, sera or blood transfusion was not a factor. In these epidemics spread has usually been traced to contact,





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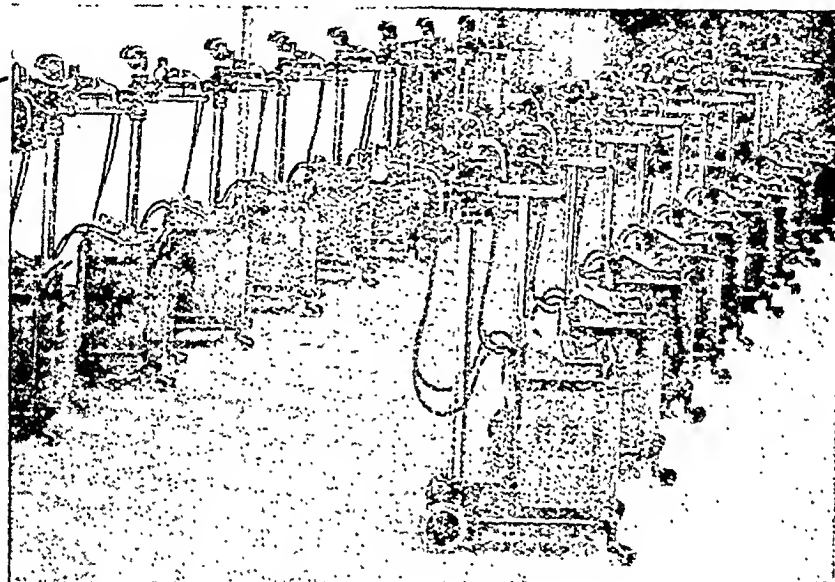


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and though in some instances it has been thought that spread may have occurred in the same way as dysentery—i.e. from faecal contamination—the majority of opinion is that infection is conveyed by droplet. The evidence in favour of droplet infection is chiefly derived from epidemiological considerations; no positive proof has been achieved. In one outbreak jaundice was associated with an epidemic of measles, in another with an epidemic of diarrhoea, but in the majority of outbreaks no such associations were found, and the conclusions from a study of contact incidence are, as stated, in favour of droplet spread. In the Middle East there is no apparent connection between the spread of infectious jaundice and that of dysentery.

A suggestion has been made that blankets and other articles may convey infection, and these, therefore, should be disinfected.

**Clinical course.**—The incubation period is usually long; estimates for the naturally occurring disease vary from 3 to 8 weeks, for the disease which follows the use of serum the period may be from 16 days to 5 months or more.

As a rule the natural disease runs a mild course, but occasional fatalities occur. There is reason to think that infection may be acquired without causing symptoms, and that symptoms resembling those of mild influenza may occur without the development of jaundice. In this case diagnosis is almost impossible, and in either case the danger of spread of infection is evident. Definite cases can be isolated; undiagnosed cases and infective persons, who are not ill, cannot. There is reason to believe that patients are infective in the pre-icteric stage, and that they may cease to be infective about a week after the onset.

Infectious jaundice usually commences gradually with headache, drowsiness, fatigue and anorexia as prodromal symptoms, going on to nausea, vomiting, some abdominal pain and possibly diarrhoea. The temperature may be raised, usually slightly, but sometimes up to 103°F., or the patient may be apyretic. The disease may start abruptly with fever. Joint pains and urticaria may be present; the liver may be enlarged and tender. The urine is dark and the stools may be pasty and light. Jaundice usually appears within a few days, but in some cases it may be the first and only symptom. The depth of jaundice varies greatly.

In fatal cases, which are rare, there may be cerebral symptoms and a rapidly fatal course, or death may take place at a late stage, possibly as a result of liver insufficiency.

In young persons the disease is more rapid in onset and course than in old people, in whom jaundice may appear late after the initial symptoms, and persist long. The period of disability, therefore, varies considerably, but even in the milder cases it usually lasts several weeks. There is evidence that the pathological process is one of necrosis of the liver cells and that in severe cases the condition resembles subacute yellow atrophy. It is therefore advisable to ensure a period of convalescence during which no strain is thrown on the liver—the damage may be permanent and cirrhosis has been recorded as a late sequel. In view of this there is a tendency to treat the disease rather more seriously than was the case when it was regarded as due to a catarrhal process.

**Treatment.**—The main principle is to relieve the liver as much as possible. Glucose is given freely by the mouth. If there are signs of liver insufficiency, 5 per cent glucose solution should at once be given intravenously, but not more than 500 c.c. in 24 hours. Administration of 5 to 10 units of insulin in the same period aids the assimilation of the glucose. Protein and fat are reduced, or in severe cases, eliminated from the diet. Rest and nursing are indicated according to patient's condition.

**Tests.**—Van Rooyen and Gordon suggest the following tests for the detection of patients who show symptoms suggesting this infection but in whom the jaundice does not appear. Such cases may occur during epidemics of infectious jaundice and are important in the spread of the disease:—

1. Examination of urine for bile and urobilinogen.
2. The intradermal histamine test (Cullinan).

'The equivalent of 0.1 mg. of histamine in a one minim solution is injected intradermally into an area of skin devoid of sunburn or freckles. After 10 minutes a wheal appears surrounded by a red zone. In good daylight, a piece of glass is pressed over the wheal and the colour of the centre compared with the colour of the skin outside the red zone. If there is a concentration of bile in the blood stream corresponding to one unit of van den Bergh (0.5 mg. per cent serum bilirubin) or more the centre of the wheal is distinctly yellow.'

3. Icterus index.

**Remarks.**—It is worth remembering that, with the present intensive use of transport, yellow fever may be conveyed to parts of the world from which it had not previously been reported. If the infection were introduced to an area in which the mosquito vector *Aedes aegypti* exists, the disease could spread dangerously. This mosquito is found in the coastal areas of Central and South America, tropical Africa, the Mediterranean and throughout the Far East. An outbreak of yellow fever could conceivably be mistaken for one of infective hepatitis. Two measures might be taken:—

1. Specimens of liver should be taken for microscopical examination from persons who have died from a disease characterized by jaundice.
2. Serum from patients who have recovered from jaundice should be examined for the presence of yellow fever protective bodies, due note being taken as to whether the patient had or had not previously been inoculated against yellow fever.

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### An Intradermal Test For Vitamin C Subnutrition

By L. B. SLOBODY, M.D.

(Abstracted from the *Journal of Laboratory and Clinical Medicine*, Vol. XXIX, May 1944, p. 464)

1. Our intradermal test, raising an approximately 4 mm. wheal with a N/300 dichlorophenol indophenol solution, will indicate vitamin C subnutrition states.

2. Of 59 patients with blood vitamin C levels below 0.3 mg., the skin test times were more than 14 minutes in 54. In 10 children on vitamin C deprivation diets, the blood levels fell, and the skin test times became prolonged. The skin test times were then reduced to normal following administration of ascorbic acid.

3. A skin test time of more than 14 minutes suggests a definite degree of body unsaturation, from 9 to 13 minutes mild unsaturation, and less than 9 minutes a normal amount of vitamin C in the body tissues.

4. Different tests give information on various aspects of the vitamin C nutritional state and thus will not always correlate. The blood level reflects only recent dietary intake. The skin test parallels the degree of body saturation. Gross and biomicroscopic changes in the gums demonstrate actual tissue changes.

### Localized Neuritis of the Shoulder Girdle

By J. D. SPILLANE, M.D. (Wales), M.R.C.P.

(Abstracted from the *Lancet*, ii, 30th October, 1943, p. 532)

**Conclusions.**—Experience indicates that there has been an increase in the incidence of brachial neuritis in civilians in Great Britain and in the incidence of

isolated paralysis of individual nerves in the upper and lower limbs of soldiers both at home and in the Middle East.

A group of 46 cases has been defined in which an unusual degree of wasting of certain muscles about the shoulder girdle of fairly rapid onset has been the characteristic clinical feature. In some cases it seems that the disability is permanent.

The causes are unknown in most cases. It is probable that most of the shoulder girdle cases belong to the same group but their relation to the isolated examples of neuritis of arm and leg is uncertain.

Civilian practitioners whom I have consulted in the Middle East have not seen such cases before and Sir James Purves-Stewart has informed me that in his capacity as consultant neurologist there in 1914-18 he did not see such cases.

### Serologic Diagnosis of Relapsing Fever

(From the *Journal of the American Medical Association*, Vol. CXXIV, 8th April, 1944, p. 1064)

The diagnosis of relapsing fever may be difficult, since the symptoms resemble closely those of other diseases with intermittent fever. If pulmonary involvement is present the symptoms may be ascribed to other acute infectious diseases. From the blood of infected mice and rats Stein (1944) has prepared a stable spirochetal antigen. Spirochæte-containing blood was laked with saponin and the spirochætes were washed well with isotonic solution of sodium chloride. Suspensions of spirochætes obtained in this way were found to act as specific antigens in complement fixation and agglutination tests with serum from patients and animals infected with spirochætes of relapsing fever. Positive reactions were not obtained with serum of patients convalescent from other infections, e.g. typhus fever, malaria, Rocky Mountain spotted fever, Weil's disease, syphilis or typhoid. Stein's antigen merits further study, since it may prove to be useful in the diagnosis of relapsing fever.

### REFERENCE

STEIN, G. J. (1944) .. *J. Exper. Med.*, 79, 115.

### Bacteriophage Therapy in Bacillary Dysentery

By J. S. K. BOYD

and

B. PORTNEY

(Abstracted from the *Transactions of the Royal Society of Tropical Medicine and Hygiene*, Vol. XXXVII, February 1944, p. 243)

1. An investigation into bacteriophage therapy in bacillary dysentery was carried out in circumstances which permitted of accurate control.

2. The bacteriophage used was of high potency. It was specific for the dysentery organisms isolated. It was recovered from the stools of patients to whom it was administered.

3. No prophylactic action was found to result from a 3-day administration of bacteriophage along the lines recommended by Kliewe and Helmreich.

4. The incidence of dysentery in a community treated with bacteriophage at the first sign of diarrhoea was no different from that in a control community.

5. Neither the severity nor the duration of the attack in the bacteriophage-treated group was dramatically less than in the controls.

6. Dysentery bacilli were recovered from the stools after the bowel had been exposed for as long as 4 days to the action of bacteriophage.

7. It is concluded that bacteriophage fails to exercise *in vivo* the potent properties which it exhibits *in vitro*.

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## Review

**FIRST AID AND SANITATION FOR TROOPS.** Published anonymously. Available from the Times of India Press, Bombay. Price not known

THIS booklet published anonymously has been written for the benefit of the Squadron, Company, Platoon Commanders and English-speaking V.C.Os and N.C.Os of the Indian Army.

It starts with a suggested syllabus of 12 days' teaching, 1½ hours each day, the 11th and 12th days being devoted to sanitation. Then follow 2½ pages on anatomy, 2½ pages on physiology, and sections on bandaging, fractures, dislocations and injuries to joints, wounds, treatment of bleeding, burns, frost-bite, shock, heat, blast injuries, artificial respiration, methods of carrying the injured, snake bites, insect stings, sanitation, flies, mosquitoes, sandflies and other insects. The lines followed are in the main those usually followed in manuals on first aid, but an attempt has been made to avoid the use of technical words and medical and first-aid jargon. The information given is usually accurate; there are occasional lapses such as the statement that the spleen supplies the cells of the blood. The book is well done. The language is fairly simple although it might be even simpler in places. It is good to see that the use of walking sticks, umbrellas, rifles, bayonet scabbards, etc., as splints is deprecated, for they do not immobilize a limb properly. There are ten illustrations mostly indicating methods of bandaging and splinting. The illustrations are good, but more of them would have been welcome. The sections on war wounds and injuries are very useful; they include directions on the removal of a wounded man from a horse, from a tank or other vehicle. A very useful book.

## BOOKS RECEIVED

1. Diseases of infancy and childhood, fourth edition, by W. Sheldon. Published by J. and A. Churchill Limited, London.
2. Psychological medicine: A short introduction to psychiatry with an appendix 'war-time psychiatry', by D. Curran and E. Guttman. Published by E. and S. Livingstone, Edinburgh. Price 10s. 6d.
3. A pocket surgery, by P. H. Mitchiner and A. H. Whyte. Published by J. and A. Churchill Limited, London.
4. Endocrine man: A study in the surgery of sex, by L. R. Broster. Published by William Heinemann (Medical Books) Limited, London. Price, 12s. 6d.
5. Treatment by manipulation in general and consulting practice, fourth edition, by A. G. T. Fisher. Published by H. K. Lewis and Company, Limited, London. Price 16s.
6. Practical anaesthetics for students, hospital residents and practitioners, by J. R. Mackenzie. Published by Baillière, Tindall and Cox, London. Price 10s. 6d.
7. Essentials of syphilology, by R. H. Kampmeier with chapters by A. E. Keller and J. C. Peterson. Published by J. B. Lippincott Company, Philadelphia and London. Price 25s.
8. The medical annual: A year book of treatment and practitioner's index, sixty-second year 1944, edited by Sir H. Tidy and A. Rendle Short. Published by John Wright and Sons Limited, Bristol. Price 25s.
9. Modern treatment in general practice: Year book 1944, edited by C. P. G. Wakeley. Published by The Medical Press and Circular, London. Price 15s.
10. Medical diseases of war, fourth edition, by Sir A. Hirst. Published by Edward Arnold and Company, London. Price 21s.
11. Vital statistics and public health work in the tropics, by P. Granville Edge. Published by Baillière, Tindall and Cox, London. Price 12s. 6d.

## Abstracts from Reports

**THE ROSS INSTITUTE OF TROPICAL HYGIENE, INDIA BRANCH. REPORT OF THE COMMITTEE OF CONTROL FOR THE YEAR ENDED 31ST JULY, 1944**

NOTWITHSTANDING the many disadvantages under war-time conditions much good work continues to be carried out by the Ross Institute in India. During the year Dr. Ramsay, the Principal of the India Branch, made an extensive tour advising on anti-malarial measures, and was of some help to the Allied Forces in the operational areas. The report includes a survey of the work carried out by the organization in different localities. It stresses the dangers of surface drains, many miles of which have been dug to prevent malaria, and insists on their filling up. Deforestation, owing to recent demand for timber, has contributed to increased incidence of malaria. Advances continue to be made in flushing methods, but perhaps the most recent one is the pipeless automatic syphon. There was an epidemic of *ulcus tropicum* in South India; malnutrition did not appear to be an important cause. Poor diets have during the past year been responsible for much sickness and increased death rates throughout India. As evident from the accounts, the financial position of the institution is sound.

**REPORT OF THE LEPROSY COMMITTEE APPOINTED BY THE GOVERNMENT OF THE CENTRAL PROVINCES AND BERAR, 1944**

THE Government of the Central Provinces and Berar appointed a Leprosy Committee on the 18th October, 1943, to consider the present leprosy problem and anti-leprosy activities in the province and to make suggestions for a future development of the work on sound lines. The following is a summary of the recommendations made by this Committee.

*The in-patient institutions.*—At present about 40 per cent of the inmates of these institutions are of the non-infective type. It is recommended that vigorous efforts should be made to greatly reduce the number of the present non-infectious patients in these institutions, and in future to admit, as far as possible, only the infective cases.

To achieve these objects the Government should make some alternative arrangement for the existing non-infectious patients who cannot possibly be discharged, and should adopt a policy of giving a capita-tion grant for future admissions only in respect of the infective cases.

The two alternative arrangements suggested for dealing with non-infectious crippled cases of leprosy are: (a) The establishment of special homes for these cases in connection with the existing institutions situated about a mile or two away. Supervision and administration of these homes could be undertaken by the administrative staff of the respective institutions. (b) The establishment of a new and separate institution in the shape of a 'Poor Home'. Possibly the establishment of a new home is a better solution, since it is likely to solve the problem of not only the non-infectious crippled cases in the institutions but also of such cases outside the institution.

*Special leprosy clinics.*—The handicaps under which these clinics work have been discussed, and it is recommended that steps be taken to remedy these defects. The following points need special attention:—

- (1) Proper accommodation should be provided for all treatment centres.
- (2) A trained assistant should be appointed at each centre to help the doctor.
- (3) Uniform printed record forms and registers be supplied to the centres.



- (4) Suitable staff quarters should be provided.
- (5) Where possible the clinics should be linked up with an in-patient institution so that leprosy patients needing temporary hospitalization for acute leprosy conditions could be admitted into these institutions.

*The clinics attached to dispensaries and hospitals.*—Arrangement should be made to impart training in leprosy to all the doctors at these clinics.

If necessary, a separate room may be provided for treatment of leprosy cases to meet the objections of other patients attending the hospital or the dispensary.

At present, of over 300 dispensaries and hospitals in the province, only about 35 have arrangements for treating cases of leprosy. It is recommended that such arrangements should be made in the remaining hospitals and dispensaries also.

*Isolation of infective cases.*—So far treatment has been given the prime importance in the anti-leprosy campaign in the province. Treatment of cases of leprosy is no doubt necessary, but the spread of the disease cannot be controlled merely by opening treatment centres. The only sure method for controlling the spread of disease is the isolation of infective cases. It is important that this fact be recognized, and due attention be paid to the isolation of infective cases.

In view of (a) the large number of infective cases in the province, (b) the limited accommodation in the existing institutions, and (c) the fact that such accommodation cannot be adequately increased due to limited financial resources, it is very essential that some alternative method of isolation be adopted. It is therefore recommended that the Government should take such isolation measures as an important feature in its future anti-leprosy campaign.

It is suggested that such village or group isolation centres should be established in connection with the existing special leprosy clinics. This work can be started in one or two such centres, and can then be gradually expanded.

It is suggested that at these centres leprosy should not be tackled as an isolated problem but should be linked up with other public health and rural reconstruction work. Each centre should be organized as a Health Unit under the charge of the Assistant Health Officer of the clinic.

*Propaganda.*—In addition to the propaganda already being done by the sub-assistant health officers, the Leprosy Specialist of the province should actively participate in this work by addressing special public meetings and by writing suitable articles in the local press.

Special importance should be given to anti-leprosy propaganda amongst school children; school books on hygiene should include a chapter on leprosy.

*Surveys.*—Leprosy surveys in an area should be undertaken only with some specific object in view and not as an end in itself.

The records of surveys should be maintained on uniform and approved printed forms.

Sample surveys should be undertaken in those parts of the province for which no definite information is available regarding the incidence of leprosy.

For a thorough and intensive survey the inclusion of a lady assistant in the survey party is considered essential.

Areas where intensive surveys and/or control measures are adopted should be re-surveyed at suitable intervals.

*Teaching.*—It is recommended that steps should be taken to ensure that the leprosy training given at the Medical School, Nagpur, becomes an essential part of the curriculum.

Further efforts should be made to organize post-graduate training at centres where adequate clinical material is available. This training should be available not only to the personnel of the Medical and Public Health Departments, but also to private practitioners.

*Medical institutions and leprosy.*—There is no justification for refusing admission into general medical

institutions to leprosy patients needing attention for other diseases. There is no adequate reason why, if needing hospitalization, non-infective cases should not be admitted to general wards, and infective cases to infective wards. It is recommended that the Provincial Government should issue administrative instructions in this connection to all the institutions under its control.

*Employment of people suffering from leprosy.*—Persons suffering from non-infectious type of leprosy should be allowed to continue in the employment of Government, local bodies or industries, etc., provided they remain under expert medical supervision, and produce periodical certificates of non-infectivity.

*School children and leprosy.*—School children suffering from the non-infective type of leprosy should not be expelled from the schools provided they remain under expert medical observation, and produce periodical certificates of non-infectivity.

*Leprosy staff.*—For the success of the anti-leprosy campaign in the province it is considered very essential that the pay, status and prospects of the workers should be such as to attract suitable men of the right calibre. It is recommended that the present Leprosy Specialist of the province should be made responsible directly to the Director of Public Health and be styled as the Provincial Leprosy Officer.

*Legal measures.*—The existing legal powers for the control of leprosy have not been of much practical value. There is a great necessity of amending the existing leprosy laws or of framing a new Act. Since the preparation of a model Leprosy Act by the Central Government is under consideration, it is recommended that the preparation of this Act should be awaited, and then suitable provincial legislation should be based on this model Act.

*Leprosy Institute of India.*—It is noted that the Central Advisory Board of Health at its fourth meeting (1942) has recommended that the Government of India should establish a Leprosy Institute of India. It is considered that all the requirements laid down for the location of the proposed Leprosy Institute are met with in this province. This Committee recommends to the Government of Central Provinces and Berar to invite the Government of India to consider the possibility of locating the future Leprosy Institute at some suitable place in the Central Provinces.

*Co-ordination between Government and voluntary organizations.*—It is desirable that there should be a spirit of co-operation and co-ordination between the various agencies, both Government and voluntary, engaged in anti-leprosy work. An encouraging feature of anti-leprosy work in the province is the coming into existence of such local voluntary organizations as Maharogi Sewa Mandal, and the Uplift Committee. It is recommended that the Government should recognize the importance of the work being done by these organizations, and should encourage them in every possible way. Further growth and expansion of similar organizations should be encouraged.

## Correspondence

### INFARCTION FOLLOWING THE USE OF AN ABORTIFACIENT

SIR,—I have read with interest the case report of infarction following the use of an abortifacient by Dr. Deshmukh in the July issue of the *Indian Medical Gazette*. He attributes the dangerous complications which followed the 'comparatively trivial operation' to the 'accidental injection of the paste in the vascular channels' and thinks that 'the disaster could, perhaps, have been avoided if the injection had been stopped as soon as the bleeding was noticed'. The dangers of the use of soft soap as an abortifacient have received frequent editorial comment in the *Journal of the*

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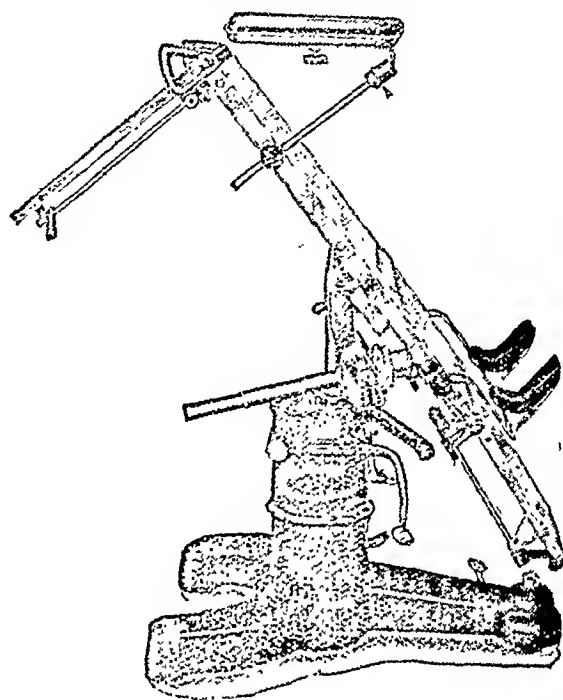
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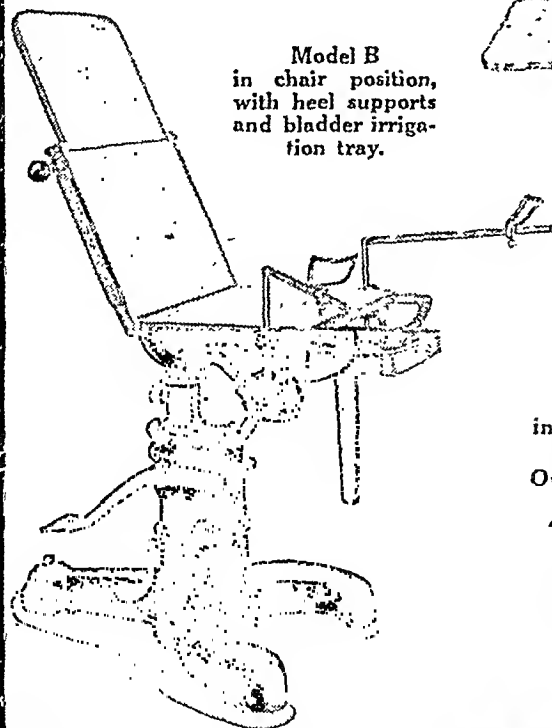
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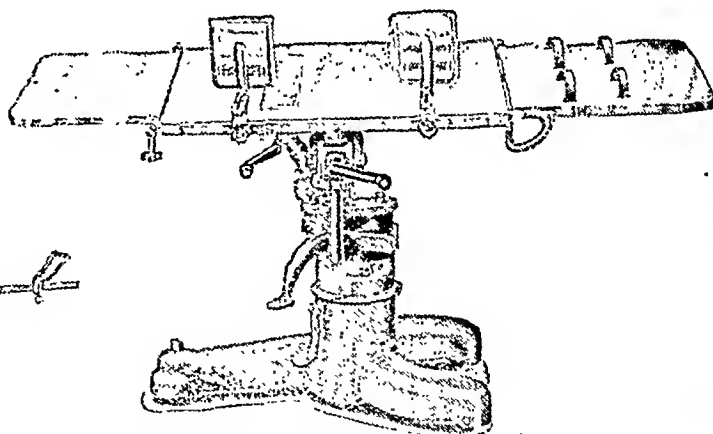
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American Chemical Association in a recent number of which (*Chemical Journal of American Medical Association*, 20th May, 1944, page 205) Weilerstein of the U.S. Food and Drug Administration has reviewed the subject under the title 'Intra-uterine pastes'. According to him, while the pastes have been reported to be ineffective in nearly 50 per cent of the cases, their use 'involves every danger which is inherent in a surgical invasion of the uterine cavity plus the added risks of introduction of a foreign body which is lost to the control of the operator when once introduced. Its apparent ease of application renders it liable for use in the hands of the inept and in the hands of practitioners who would not attempt abortion by other means'. There is the additional 'danger of a chemical irritant which can spread beyond the point where it is introduced, and throughout the uterine cavity or enter the blood stream, initiating dangerous phenomena' such as hæmolytic, pulmonary embolism, generalized septicæmia, hæmorrhage and inflammation with its sequelæ, e.g. sterility due to tubal occlusion, peritonitis and necrosis of the uterine wall, some of these conditions often proving fatal. He concludes with the statement that 'appropriate steps have been taken to control this situation by the institution and successful completion of legal actions directed at the manufacturers of these products under the Federal Food, Drug and Cosmetic Act'.

There is reason to suppose that similar products are being used in a considerable number of cases in India also, and in the light of the expert opinion, their use is strongly to be deprecated. In order to bring these facts before the Indian medical profession, I wish you would publish in the *Indian Medical Gazette* this note or an abstract of the American paper.

[The writer of this letter wishes to remain anonymous.—EDITOR, I.M.G.]

#### EPIDEMIC OF TYPHOID FEVER IN SURAT

SIR,—I wish to draw your attention to the following, with a view to seeking your guidance in the matter:—

There is at present a severe epidemic of typhoid fever in Surat. A large number of cases develop multiple complications, and the mortality seems to be fairly high.

During the last three weeks I saw three cases, one on the 28th day, one on the 19th day, and one on the 22nd day of the illness, each one with a varying degree of hepatic enlargement.

In each case the liver has been more than three fingers below the right costal arch.

The one seen on the 28th day had also an enlarged and tender gall-bladder.

This hepatic enlargement has been extremely tender and painful, causing marked restlessness and hiccup, nausea, eructations, vomiting, etc.

In two of the three cases, a vague history of a previous dysenteric infection could be elicited. Not one was treated for a proved amœbic infection before. Only one of the three had a painful enlargement (one finger) even during the earlier days of the recent illness. He showed a gradual enlargement of a lump going down from the right hypochondrium to the right lumbar area, almost reaching the right iliac fossa, and going medially to the left of the midline.

There was œdema of the skin, high fever and high pulse rate, and a leucocyte count of 7,600; polymorphonuclears 78 per cent per c.mm. with lymphocytes 20 per cent, monocytes 2 per cent and no eosinophil.

Six leeches were applied with a view to lessening hepatic congestion. Three injections of pyelopurin (Cipla) 5 c.cm. with glucose 25 per cent 25 c.cm. were given intravenously during a period of three days.

This relieved the pain a little, though not to the desirable extent. Since the swelling was very tender and almost pointing at one spot, a wide-bored exploration needle was used for liver puncture but no pus could be found.

With some hesitation, since the circulation was not very satisfactory, three injections of emetine hydrochloride  $\frac{1}{2}$  gr. each with coramine 1.7 c.cm. were given,

one injection every day, intramuscularly. The pain, tenderness, swelling, etc., subsided, the temperature returned to normal and remained so for a week, though the general condition of the patient suggested a picture of extreme exhaustion. The blood pressure was 110/68 mm. of Hg., pulse 82 per minute, temperature 97°F., respiration 22 almost for a week.

It was difficult to decide what exactly improved the patient's condition, though surely  $1\frac{1}{2}$  grains of emetine hydrochloride (in 3 days) could not have done the trick. More emetine was not given, as the patient looked low and he had no complaints at all.

The other two patients seen on the 19th and 22nd day were given similar treatment without any benefit.

I have made careful attempts to ascertain that these tender large livers were not due to a congestive cardiac failure or malaria.

I am told by other practitioners in the town that they have been seeing a severe hepatitis occurring as a complication during enteric fever, not responding to ordinary methods of treatment.

Cholecystitis is a very well-known complication of typhoid fever, with a definite line of treatment to go by; not so, the type of hepatitis, one is at present seeing. I would like to know, if 'hepatitis' has been a feature of some particular virulent strain of *B. typhosus* infection. Has it been recognized as a feature of epidemics elsewhere as in the present case?

In the event of a proved amœbiasis, would you advocate a full course of emetine during the third or fourth week of enteric fever bearing in mind the low cardiac reserve in most of the cases?

I wish to point out with some regret that all the three cases reported here died. The first one died of acute cardiac failure on the 52nd day; the second of septicæmia following an infected bed sore, and the third one of hæmorrhage and perforation.

It is hoped that you will kindly throw some light on the difficulties we are facing here, and oblige.

R. K. DESAI, M.D. (Bom.).

KANPITH, SURAT,  
17th September, 1944.

[Note.—The editor has no experience of hepatitis complicating typhoid and feels quite unable to comment on this letter.—EDITOR, I.M.G.]

#### NAGA SORE IN JAMNAGAR

SIR,—Naga sore as the name indicates was mainly prevalent in Assam (India) and some of the factors which favour its occurrence, it appears, are the heavy rainfall there and the mode of living of the people who suffer most from this condition.

The occurrence of Naga sore in Jamnagar this year throws some light on its causation; the epidemic of Naga sore has appeared among the class of people (not necessarily poor) who, during a heavy rainy season, walked in mud and worked in marshy localities, barefooted. Forty-five inches of rain, mud and marshy conditions—and Naga sore were not previously known to this place.

The same thing happened in Benares last summer, when heavy rainfall flooded the area, resulting in mud and marsh so that Naga sore broke out in epidemic form.

SANTOKH SINGH,  
In-charge Laboratory.

IRWIN HOSPITAL,  
JAMNAGAR,  
15th September, 1944.

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Butterworth and Co., Ltd., London.

## CHLOROFORM IN CASES OF SCORPION BITE

Sir,—Sometime ago—probably some years ago—one of your correspondents recommended chloroform in cases of scorpion bite. I am not able to give you the exact reference, nor can I quote the writer's own words. But I remember to have read that those who came crying went away with smiling faces.

I am sorry to inform you that this has not been my experience. I have tried whiffs of chloroform in half a dozen cases without success. I hesitated, however, to report my negative results because of the paucity of cases.

Recently, however, my own baby was stung by a scorpion. I gave him whiffs of chloroform and within two minutes he went under. The anaesthesia lasted for about ten minutes. Only for this short while was the child quiet. As soon as he came round, he began to cry as loudly as before, and the pain and suffering were as intense as ever. After about 3 hours, exhausted by crying and probably relieved by some local application that we had tried, he went to sleep. Chloroform had completely failed to relieve him.

I did not inject novocain locally because it has only a temporary effect. I had read about the efficacy of a 2 per cent solution of sodium bicarbonate, but did not try it as I had no personal experience of it.

K. A. SHAH, M.B., D.S.

RANCHHODLAL DISPENSARY,  
PANCHKUWA, AHMEDABAD,  
9th October, 1944.

[Note.—In the editor's opinion the one and only treatment for scorpion bite is an injection of morphine. This treatment he applied in himself with most satisfactory results.—EDITOR, I.M.G.]

VITAMIN-B<sub>1</sub> DEFICIENCY

Sir,—While reading in your issue of July 1944 the article on Polyneuritis and on vitamin-B<sub>1</sub> deficiency I was reminded of another case of vitamin-B<sub>1</sub> deficiency. The patient was aged 50. He neither smoked nor drank.

He suffered from indigestion some 30 years ago which was diagnosed as sprue and treated as such. He had been a vegetarian from childhood, but after this he took meat diet for about 8 years and then resumed a vegetarian diet. During these 30 years he has suffered from no other ailment.

Of late he has been getting unsteady in his gait. Romberg's sign was present. Light weight and cotton-wool sensations of his whole body had disappeared. Going down the stairs was indeed a great exertion, specially at night in darkness. He suffered from partial impotence. The most recent development noticed by him was the beginning of atony of his bladder, i.e. the force of his urination began to decrease.

His mental condition was normal. His digestion was nearly normal, his only complaint being slight distension. His urine was normal. The blood showed a slight anaemia.

He was given 10 mgm. of vitamin B<sub>1</sub> every other day. His last symptom disappeared with the first injection. His impotence disappeared after 2 or 3 injections. The dose of vitamin B<sub>1</sub> was increased to 50 mgm. twice a week. Light weight and cotton-wool sensation are beginning to appear. The distension of his stomach has gone. He had noticed bleeding from his gums when rubbed for some years past; this also is beginning to disappear. He has taken to meat diet.

HIRANAND DIVANISING, M.B., D.S.

HYDERABAD, SIND,  
11th September, 1944.

## SYPHILITIC MELANOSIS

Sir,—I am referring to a paper on p. 172 of the *Indian Medical Gazette*, April 1944, on 'Syphilitic melanoderma' where you state that in Becher and

Obermayer no mention is made of syphilis as a cause of melanosis. In my book 'Histologie der Hautkrankheiten' Springer Verlag, Berlin 1925, Vol. I, p. 517, I do mention it and refer to Fourrier and to Unna as describing it as a rare type of the disease. One case was published in *Archiv. f. Dermatologie und Syphilis*, Vol. 132, in 1921, by P. Unna, Jr.

O. GANS, M.D.

19th September, 1944.

## A CASE OF BENIGN TERTIAN MALARIA

Sir,—I shall be much obliged if you will kindly publish the following case notes in your valuable *Gazette* with a view to ascertaining if similar cases have been experienced by any of your readers.

A Mohammedan lady was under my treatment for malaria (B.T.). On 16th June, 1944, she had a temperature of 103°F. Quinine mixture containing quinine sulphate gr. vii was given thrice daily for the first day. From the second day, there was no temperature and I prescribed quinacrine—1 tab. thrice daily. On the night of the sixth day of quinacrine treatment, which was the last day of the course, she developed delirium with periods of crying, singing, incoherent talking, etc. This delirium lasted for 5 days but gradually improved with the following treatment. I noticed yellow discoloration of the skin and mucous membrane on the seventh day which simulated atebria discoloration.

*History of the case* :—She suffered from malaria twice last year. She gave birth to a healthy living child 3 months ago.

*Physical examination* :—Heart and lungs—nothing particular. Liver and spleen—not enlarged.

*Treatment* :—Morphine and atropine injection for the night. Calomel gr. iii at bed time followed by saturated solution of mag. sulphi. 1 oz. next morning. Peacock's bromide  $\frac{1}{2}$  dr. t.d.s. afterwards. Then a chologogue mixture and a diuretic mixture were prescribed.

The patient recovered her normal senses but there are still signs of pigmentation of the skin, i.e. 22 days after the administration of quinacrine.

It would be interesting to know if any of my medical friends have had a similar experience with such a case and if the administration of quinacrine is likely to have caused such symptoms, as the patient is normal in every way.

N. BAROOAH, L.M.P.

Assistant Medical Officer.

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10th July, 1944.

[Note.—Cases of mental disturbance are not infrequently seen in malaria, and also mental disturbance has been recorded as a result of treatment with atebria or its equivalent, mepacrine or quinacrine.—EDITOR, I.M.G.]

## Service Notes

## APPOINTMENTS AND TRANSFERS

In exercise of the power conferred by clause (a) of sub-section (1) of section 3 of the Indian Medical Council Act, 1933 (XXVII of 1933), the Central Government is pleased to nominate Lieutenant-Colonel P. H. S. Smith, O.B.E., M.B., B.S., (Dub.), I.M.S., Officiating Inspector-General of Civil Hospitals, North-West Frontier Province, to be a member of the Medical Council of India from the North-West Frontier Province, with effect from the 5th October, 1944, *vice* Colonel J. P. Huban, I.M.S., resigned.

In exercise of the power conferred by clause (a) of sub-section (1) of section 3 of the Indian Medical Council Act, 1933 (XXVII of 1933), the Central Government is pleased to nominate Colonel A. H. Hartley,

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C.I.E., M.B. (Q.V. Canada), M.R.C.S., I.M.S., Inspector-General of Civil Hospitals, Central Provinces and Berar, to be a member of the Medical Council of India from the Central Provinces and Berar, with effect from the 27th October, 1944, *vice* Dr. M. R. Cholkar.

Lieutenant-Colonel P. A. Dargan, I.M.S. (Retd.), Civil Surgeon, New Delhi, was appointed to hold charge of the duties of the post of Chief Medical Officer and Civil Surgeon, Delhi, in addition to his own duties, with effect from the 4th September, 1944, *vice* Lieutenant-Colonel R. McRobert, granted leave.

Lieutenant-Colonel De Lisle Carey was appointed to officiate as Officer on Special Duty in the Medical Division of the Directorate General of Supply for a period of 10 days, with effect from the 28th August, 1944. He has been appointed to officiate as Director (Instruments and Appliances) in the same Directorate General, with effect from the 7th September, 1944, *vice* Major R. I. Reid, reverted to Army Duty.

Major C. K. Lakshmanan, Officiating Director of Public Health, Bengal, is appointed Additional Director, All-India Institute of Hygiene and Public Health, Calcutta, with effect from the 27th September, 1944.

The services of Major M. Jafar, Officiating Chief Health Officer, Delhi, are placed temporarily at the disposal of the Government of Bengal for appointment as Director of Public Health, Bengal, with effect from the afternoon of the 23rd September, 1944.

Major B. N. Khan, Additional Chief Health Officer, Delhi, is appointed to officiate as Chief Health Officer, Delhi, with effect from the afternoon of the 23rd September, 1944.

On return from leave Major J. H. Caverhill is appointed as Resident Medical Officer, Presidency General Hospital, Calcutta, *vice* Dr. P. N. Ray, granted leave.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS  
(Emergency Commissions)

To be Captains

David Satya Nand. Dated 20th February, 1943.  
Suraj Prakash. Dated 15th August, 1944.  
Prem Singh. Dated 20th August, 1944.  
(Miss) Shanta Jayawant. Dated 29th August, 1944.

14th July, 1944

Rameshwar Dayal Gupta.  
Jagat Durlav Bhattacharyya.  
Nirmal Chandra Dutta Gupta. Dated 29th July, 1944.  
Vulugundam Lakshminarayana Rao. Dated 6th April, 1942.

Arun Kumar Gupta. Dated 3rd September, 1942.  
Bramwell Richmond Sukh. Dated 10th May, 1944.

21st July, 1944

Dhrubendu Mohan Kar. Gangasani Janardan Reddy.  
Mohammad Sabir Mullick. Dated 12th July, 1944.  
Atmaram Rao Gulvadi. Dated 14th July, 1944.

(WOMEN'S BRANCH)

To be Captains

Miss Leela Bhagwandas. Dated 23rd July, 1944.  
Miss Annie Myrtilla Pichaimuthu. Dated 24th July, 1944.

To be Lieutenants

1st July, 1944

Hari Prasad Vaishnava.  
Mohammad Anisur Rahman Khan.

13th July, 1944

Mohamad Shuaib. Mohammad Bashir Azami.

14th July, 1944

Mohammad Aslam Khan.  
Syed Ahmad Raza Peerzada.  
Mohammad Abdul Mughni.

15th July, 1944

Syed Nasir Husain Abidi.  
Mahammed Azhar-ul-Haque Siddiqi.

19th July, 1944

Sunil Ranjan Chatterji. Satya Saran Chatterjee.

20th July, 1944

Choudhary Mohammed Yasin.  
Khawaja Zaffar-ul-Aziz.  
Kartar Singh Rai.  
Syed Muzaffar Ali Bokhari.  
Yag Datt Rishi.  
Ved Prakash Sharma.  
Om Prakash Mudhok.  
Om Prakash Kapur.  
Jaswant Singh Puri.  
Om Prakash Chhabra.  
Choudhry Mohammad Akram.  
Tajuddin Ahmad Mirza.  
Shaikh Dawood Ibrahim Herekar.

21st July, 1944

Ernest Austen Sinclair. Shankat Ali Syed.  
Aman Ullah Khan. Bhisham Parkash Gupta.  
Mohammad Abdul Mannan. Dated 22nd July, 1944.  
Tarlok Singh. Dated 26th July, 1944.  
Tarlok Chand Prabhakar. Dated 8th July, 1944.  
Survapalli Pithiah Benjamin. Dated 18th July, 1944.  
Dhian Singh. Dated 3rd April, 1943.  
Mohammed Shafi. Dated 3rd April, 1943.  
Bhagwan Das Paika. Dated 5th February, 1944.  
Herbert Mangya Htang. Dated 4th July, 1944.  
Bachan Singh. Dated 13th July, 1944.  
Bhagwati Prasad Panday. Dated 15th July, 1944.  
Dayal Singh. Dated 8th August, 1944.  
Palayur Ramaswami. Dated 14th August, 1944.

15th August, 1944

Sukumar Dutta.  
Sudhansu Bhusan Nandy.  
Vinayak Ramchandra Phatak.  
Atul Chandra Chakravarty.  
Birendra Chandra Bhattacharya.

16th August, 1944

Suresh Chandra Mohapatra.  
Banshidhar Hota.  
Pashupati Nath Verma. Dated 17th August, 1944.

18th August, 1944

Ranjit Kumar Gupta. Amiya Kumar Mallik.  
Abdur Rahaman Shaikh. Dated 19th August, 1944.  
Nazrul Hasan Khan. Dated 21st August, 1944.  
Miss Churia Sarojini. Dated 28th April, 1944.  
Brajnandan Prasad Singh. Dated 11th August, 1944.  
Bimal Chandra Banerji. Dated 14th August, 1944.  
Devendra Nath. Dated 15th August, 1944.  
Cyril Ashley Hanson. Dated 16th March, 1943.

19th August, 1944

Sukhendra Kumar Chakraborty.  
Dig Bijoy Sen.  
Nirad Baran Sarkar.

20th August, 1944

Santosh Kumar Ghosh.  
Ramaswamy Iyengar Rangachar.  
Yashwant Govind Inamdar. Dated 23rd August, 1944.

Syed Ali Ahmad Sami. Dated 12th June, 1944.  
Fakhrul Hasan. Dated 11th August, 1944.  
Kunju Karunakaran. Dated 17th August, 1944.  
Bryan Eric George Garson. Dated 24th August, 1944.

27th August, 1944

Patrick John Kennedy. Duncan Eric Jeremiah.

James Thomas Marshall.

Ponduri Venkata Ramanarao. Dated 14th July, 1944.  
Sarvan Lal Chandha. Dated 20th July, 1944.  
Milik Singh Kherra. Dated 13th August, 1944.  
Sureshwar Prasad Jha. Dated 17th August, 1944.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN  
ARMY MEDICAL CORPS  
(Emergency Commission)

To be Lieutenant

(WOMEN'S BRANCH)

(Miss) Anna George. Dated 17th August, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
FOR SERVICE WITH THE ROYAL INDIAN NAVY

(Emergency Commissions)

To be Lieutenants

Eric Alfred Corbett. Dated 29th August, 1944.  
Edgar Saldanha. Dated 4th September, 1944.

The undermentioned I.M.S. (E.C.), seconded to I.A.M.C., officers revert from I.A.M.C. and are seconded for service with the Royal Indian Navy:—

Captain B. P. Srivastava. Dated 12th September, 1944.

15th September, 1944

Lieutenant A. U. Khan. Lieutenant S. A. Syed.

PROMOTIONS

Majors to be Lieutenant-Colonels

3rd September, 1944

A. Rosenbloom. C. A. Bozman.  
W. Scott. M. P. Courroy.  
W. J. Shipsey. Dated 1st October, 1944.

INDIAN LAND FORCES—INDIAN MEDICAL SERVICE  
SECONDED TO THE INDIAN ARMY MEDICAL CORPS

(Emergency Commissions)

Captains to be Majors

K. K. Patel. Dated 17th May, 1943.  
P. N. Bagchi. Dated 16th April, 1944.  
K. B. Chowdhury. Dated 10th July, 1944.  
N. C. Chatterjee. Dated 1st August, 1944.  
I. Malik. Dated 5th August, 1944.  
A. L. Sutherland. Dated 15th August, 1944.  
S. Pichumani. Dated 15th August, 1944.  
I. H. B. Ghosh. Dated 28th August, 1944.  
R. C. Bose. Dated 14th September, 1944.  
R. D. Ayyar. Dated 7th October, 1944.

Lieutenants to be Captains

C. A. Hanson. Dated 16th March, 1944.  
E. G. Clarkson. Dated 2nd July, 1944.  
W. B. James. Dated 29th July, 1944.  
G. M. Muller. Dated 6th August, 1944.  
G. De V. Merriman. Dated 12th August, 1944.

12th August, 1944

S. F. D'Costa. D. A. I. Gibson.  
D. A. H. Walton. Dated 18th August, 1944.

22nd August, 1944

J. M. F. D'Mellow. E. J. G. Cullen.  
A. R. Khan. Dated 3rd September, 1944.  
S. P. Das Gupta. Dated 6th September, 1944.  
D. K. Mitra. Dated 7th September, 1944.  
V. B. Naidu. Dated 9th September, 1944.

12th September, 1944

S. N. Datta. H. C. Chakravarti.  
S. K. Ghose. S. Chaudhuri.

G. A. D. Vaz.

17th September, 1944

P. K. Bose. R. N. Datta.  
S. N. Sen Gupta. C. R. Rangoji Rao.

A. K. Biswas. Dated 22nd September, 1944.  
S. N. Ghei. Dated 24th September, 1944.  
N. V. Doyle. Dated 30th September, 1944.

3rd October, 1944

S. K. Das Gupta. C. B. Andrade.  
E. J. Newton. Dated 14th October, 1944.  
A. D. S. McLaughlin. Dated 16th October, 1944.  
A. R. Coshan. Dated 19th October, 1944.

27th October, 1944

P. Sarvothamyya. S. K. Sen.

28th October, 1944

K. N. Sen Gupta. D. Kundu.  
S. K. Mitra. Dated 27th October, 1944.

INDIAN MEDICAL SERVICE—SECONDED TO THE INDIAN  
ARMY MEDICAL CORPS

(Emergency Commission)

Lieutenant to be Captain

(WOMEN'S BRANCH)

Miss S. C. Thomas. Dated 11th September, 1944.

INDIAN MEDICAL SERVICE

SECONDED FOR SERVICE WITH THE INDIAN AIR FORCE

(Emergency Commission)

Lieutenant to be Captain

D. K. Ray Chaudhuri. Dated 9th September, 1944.

SECONDED FOR SERVICE WITH THE ROYAL INDIAN NAVY

(Emergency Commissions)

Lieutenants to be Captains

P. F. D'Mellow. Dated 1st July, 1944.

N. Braganza. Dated 5th July, 1944.

K. M. Herd. Dated 17th July, 1944.

LEAVE

Lieutenant-Colonel F. J. Anderson, I.M.S. (Retd.), Professor of Surgery, Medical College, Calcutta, is granted leave for the period from 14th October, 1944 to 24th November, 1944.

RELINQUISHMENT

Captain Prakas Chandra Sen. Dated 1st October, 1944, on grounds of ill health.

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